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Ursula Schmidt-Erfurth
Thomas Kohnen
Editors

Encyclopedia of Ophthalmology

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With 453 Figures and 34 Tables

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Preface

Encompassed with comprehensive and focused information, accompanied by high-quality images, detailed tables, and graphics on all relevant ophthalmic topics, the *Encyclopedia of Ophthalmology* is a valuable resource for practicing ophthalmologists from the various ophthalmic subspecialties. This comprehensive source of ophthalmological expertise will also be of interest to optometrists, orthoptists, opticians, low vision specialists, researchers, residents, medical students, nurse practitioners, and all other eye care professionals who deal with the anatomy, physiology, and diseases of the eye.

The reader will benefit from the knowledge of leading experts in the rapidly changing field of ophthalmology with an easy reference, geared to provide detailed, timely, and relevant information about the rapid advances that continuously influence the field of ophthalmology. Intended as a user-friendly reference, available in hardcopy and electronic format and continuously updated. We hope that this encyclopedia facilitates easy reference and clinical use.

Acknowledgment

We would like to extend our thanks to the many authors who devoted an extensive amount of time in contributing to the development of this comprehensive coverage of current state-of-the-art knowledge in ophthalmology. We would also like to thank the consultants at Springer Nature for their commitment to publishing this book.

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Ursula Schmidt-Erfurth is Professor and Chair of the Department of Ophthalmology at the University Eye Hospital, Vienna, Austria, one of the largest academic institutions in ophthalmology in Europe. Professor Schmidt-Erfurth's clinical activities include surgical and medical retina. Her scientific research focuses on the development of novel diagnostic techniques, e.g., retinal imaging and novel treatment strategies such as intravitreal pharmacotherapy. She has founded the Vienna Study Center (VSC), which serves as the principal site for multicenter clinical trials, and the Vienna Reading Center (VRC), an independent institution for digital imaging performing image analysis for over 140 clinical sites worldwide. She is Head of the OPTIMA project, which is a continuation in the development of advanced image analysis (Christian Doppler Laboratory for Ophthalmic Image Analysis). Professor Schmidt-Erfurth is a member of many professional organizations, including the Association for Research in Vision and Ophthalmology (ARVO), Macula Society, Retina Society, Gonin Club, the European Academy of Ophthalmologists, and the American Academy of Ophthalmology. She currently serves as President of EURETINA (European Society of Retina Specialists), the largest community of retinologists worldwide. The author of over 260 original articles, Professor Schmidt-Erfurth is on the editorial board of the *British Journal of Ophthalmology* (BJO), the *Investigative Ophthalmology & Visual Science* (IOVS), and others. Professor Schmidt-Erfurth has received numerous grants and awards, among others the Research Award by the German

Ophthalmological Society, the Achievement Award of the American Academy of Ophthalmology, the Roger Johnson Award by the University of Washington, and the Donald Gass Award of the Retina Society. Since 2014, she holds an appointment as Adjunct Professor at Northwestern University, Feinberg School of Medicine, Chicago.

Thomas Kohnen M.D., Ph.D., FEBO is Professor and Chairman of the Department of Ophthalmology, Goethe-University, Frankfurt, which is one of the busiest teaching hospitals in Germany. He leads a team that helps over 35,000 patients annually and is highly active in teaching and research. He is Visiting Professor of Ophthalmology at the Cullen Eye Institute, Baylor College of Medicine, Houston, USA.

He originally studied medicine in Germany, Italy, India, and the USA before specializing in ophthalmology in 1989. After his residency, he was awarded a 2-year scholarship from the German Research Foundation to study at the Cullen Eye Institute in 1995/6 and gained an additional degree in Healthcare Management in 2006/7. During his career, he has worked both as a physician and as a scientist. This dual approach to the clinical and research aspect of the job is one he continues to be passionate about today.

A leading expert in the anterior segment, he specializes in cataract, IOL, refractive, and cornea surgery as well as treating glaucoma and retinal problems to increase optical quality. His research focuses on intraocular lenses, laser technology and cataract, and refractive and corneal surgery. He publishes and holds lectures worldwide regularly on these subjects.

He is Editor of the *Journal of Cataract and Refractive Surgery*, Associate Editor of *Der Ophthalmologe*, Focal Topic Editor of *Klinische Monatsblätter für Augenheilkunde*, Editorial Board Member of *Graefe's Archive for Clinical and Experimental Ophthalmology*, and frequently peer-reviews for top journals. He has received several awards including the AAO Lifetime Achievement Honor Award in 2002. Prof. Kohnen holds senior Board positions for a number of professional organizations including President and Treasurer of the DOG (Deutsche Ophthalmologische Gesellschaft) and is Past President of the DGII (Deutschsprachige Gesellschaft für

Intraokularlinsen-Implantation, interventionelle und refraktive Chirurgie). Elected Treasurer and Executive Board Member of the ESCRS (European Society of Cataract and Refractive Surgeons) and also the current Treasurer of the IIIC (International Intraocular Implant Club).

Research Funding: Abbott, Alcon, Hoya, Oculentis, Oculus, Schwind, Zeiss; Consultant or Advisory Board: Abbott, Alcon, Geuder, Oculus, Schwind, STAAR, TearLab, Thieme Compliance, Ziemer, Zeiss.

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A

Abbe Number

► Dispersion: Definition

Abducens Nerve

► Cranial Nerve VI (Abducens Nerve)

Abducens Nerve Palsy

► Sixth Nerve Palsies

Aberrant Lash

► Distichiasis: Definition

Aberration Free Intraocular Lenses

► Aspherical Intraocular Lens

Aberrometry

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Synonyms

Wavefront measurement; Wavefront sensing

Definition

Method for measurement, visualization, and analysis of the wavefront error of the eye.

Purpose

Aberrometry is used to quantify and visualize the wavefront error (monochromatic aberrations) of the eye.

Principle

The common principle of aberrometry is the comparison of a test figure imaged by the eye with a reference figure. From the difference, the wavefront error can be computed. The most widespread used aberrometer is the *Hartmann-Shack*

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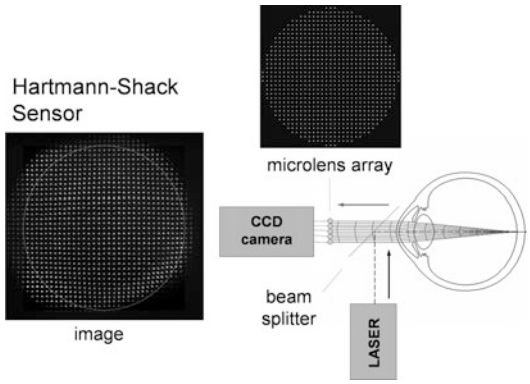

Aberrometry, Fig. 1 The principle of Hartmann-Shack Aberrometry

sensor (Liang et al. 1994). This system uses a laser beam that is reflected by the retina. The reflected light emerging from the eye is refracted into a spot pattern by a microlens array. The image of the spot pattern is caught by a CCD camera (Fig. 1). The deviation of the spots from a reference pattern is proportional to the wavefront deformation. The *aberrometer according to Tscherning* projects a spot matrix onto the fovea. The retinal image is documented by a CCD camera. Similar to Hartmann-Shack aberrometry, the wavefront error is calculated from the dislocation of the spots of the pattern. Ray tracing aberrometers apply a similar principle: a laser beam is projected onto the retina through different pupil locations sequentially. The deviation between measured and reference spot position is proportional to the slope of the wavefront in the pupil region represented by the ray. *Dynamic retinoscopy* uses – similar to retinoscopy – a light beam that is projected onto the retina. In contrast to conventional streak retinoscopy, the light beam is a laser beam that covers only a small pupil area. Thus, from local refraction data the entire wavefront error can be reconstructed.

For all aberrometers, the maximum pupil diameter for reconstruction is the pupil diameter at which the measurement was performed. While the wavefront error can be reconstructed mathematically for smaller pupils, a reconstruction for larger pupil diameters than the actual pupil diameter involves extrapolation and should be avoided.

Like all sensitive biometric measurements, aberrometry is subject to fluctuations due to tear film dynamics and microfluctuations of accommodation (Zhu et al. 2004; Montes-Mico 2007). Therefore, for clinical use it is recommended to calculate a mean value from several single measurements. For interpolation between the data points and for quantification of the wavefront error, typically Zernike polynomials are used (Thibos et al. 2002). The aberrometer software returns the Zernike coefficients as metrics of the wave aberration. From the Zernike coefficients, further image quality metrics and qualitative wavefront error representations like wavefront maps, point spread function, and convolution simulation images can be calculated.

Indication

Measurement of the entire optical properties of the eye, e.g., in preparation of wavefront-guided corneal laser refractive surgery and for the diagnostics of optical disturbances. Aberrometry is an important objective method for quantification of optical image quality for scientific purposes.

Contraindication

Aberrometric measurements are noninvasive. There are no contraindications.

Advantage/Disadvantage

In contrast to corneal topography, aberrometry allows measurements of the optical properties of the whole eye. Measurements could be taken easily without major discomfort for the patient. For maximum information, pupils need to be dilated. Aberrometry does not return valid results in case of optical media opacities (e.g., epithelial irregularities in dry eye, corneal scars, and cataract). Aberrometric measurements involving a Zernike reconstruction contain interpolated data. Modern devices combine a topographer and aberrometer within one unit. This combination allows the differentiation between corneal and lenticular origin of aberrations.

Cross-References

- ▶ Corneal Topography
- ▶ Higher-Order Aberrations, Refractive Surgery
- ▶ Refractive Surgery
- ▶ Wave Front Analysis

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Ablatio Retinae

- ▶ Retinal Detachment

Abscesses, Orbital

- ▶ Orbital Cellulitis

Absorption, Light, Spectra of Visual Pigments

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Definition

The first step of the visual process is the absorption of light by visual pigment molecules that are located in membranous disks of the outer segments in the rod and cone photoreceptors. Light absorption by the visual pigment molecules triggers a cascade of enzymatic reactions called "the phototransduction process" leading to changes in the electrical potential across the plasma membrane of the photoreceptors. Once light-induced electrical event occurs, the electrical activity is transmitted via chemical and electrical synapses to second-order (horizontal cells and bipolar cells) and then to third-order (amacrine cells and ganglion cells) retinal neurons. The ganglion cells transfer electrical activity to the brain via the optic pathways for further processing leading eventually to visual perception.

Light absorption by any medium follows a basic physical rule called the Beer-Lambert law and obeys the following relationship $I_\lambda = I_{0\lambda} * e^{-\alpha(\lambda)cl}$ where light transmission through the absorbing medium I_λ depends upon light intensity $I_{0\lambda}$ reaching the absorption medium, the absorption spectrum of the medium $\alpha(\lambda)$, the concentration c of the light-absorbing elements, and the length, l, of the light path through the medium. In the case of vision, the absorbing elements are the visual pigment molecules that are located in the outer segments of the photoreceptors. Therefore, the factors determining light absorption are the following: the intensity of light reaching the photoreceptors' outer segments (I_0), the concentration of the visual pigment molecules (c), the wavelength of light (λ), the length of the outer segments (l), and the absorption spectrum of the visual pigments (α).

The visual pigment molecules in the vertebrate retina, including human, are composed of two molecules, a protein and vitamin A derivative which in the case of mammals and humans is the 11-cis retinaldehyde (11-cis retinal). When a visual pigment molecule absorbs light, a chain of enzymatic reaction is triggered leading to an electrical signal, which starts the visual process, and the visual pigment molecule dissociate into its components; however, the chromophore 11-cis retinal is transformed into all-trans retinol. Regeneration of the visual pigment requires transformation of all-trans retinol to 11-cis retinal, a process occurring in cells of the retinal pigment epithelium.

A visual pigment is characterized by an absorption spectrum describing the probability of absorbance of monochromatic light that reaches it. The absorption spectrum reflects the interactions between 11-cis retinal and the specific protein. In the normal human retina, there are four types of photoreceptors that can be separated by the absorption spectrum of their visual pigments. Rod photoreceptors, determining vision in darkness and dim illumination, contain a visual pigment with absorption maximum at about 500 nm. Day vision depends upon three types of cone photoreceptors that differ in the absorption spectrum of their visual pigments, having absorption maxima around 450 nm, 530 nm, and 560 nm.

Disturbance in vision can reflect reduced absorption of light by the photoreceptors. According to the Beer-Lambert law, this can reflect (i) reduction in the light reaching the retina due to opaque ocular pathways (mature cataract, vitreous hemorrhage), (ii) abnormal absorption spectrum (mutation in the genes coding visual pigments), (iii) reduced concentration of visual pigment molecules (vitamin A deficiency), or (iv) shortening of outer segments (certain cases of RP).

Cross-References

- ▶ Color Vision, Three Cone Opsins
- ▶ Frequency of Light Wave
- ▶ Photoreceptor Cells

ACCC–OC

▶ Anterior Optic Capture

Accessory Lacrimal Glands

▶ Glands of Krause, Glands of Moll, Glands of Wolfring, Glands of Zeis

Accommodating Intraocular Lens

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Synonyms

Accommodative intraocular lens

Definition

An accommodative IOL is an artificial intraocular lens which is designed to enable accommodation (a dynamic change in focus of the eye).

Indication

Accommodating IOLs are supposed to transform the movement of the ciliary muscle which occurs with an accommodative effort into a dynamic change of dioptric power of the eye. They are indicated to treat the loss of the ability to accommodate which occurs with advancing age (presbyopia).

Contraindications

Accommodative IOLs are not indicated in eyes with a weakened zonule and insufficient fixation of the crystalline lens capsule.

Techniques and Principles

All accommodating IOLs currently available are based on the principle of translation of the IOL optic. By means of a hinge or a similar mechanism in the IOL, haptic contraction of the ciliary muscle is expected to effect an anterior shift of the IOL optic

and thus increase the power of the eye. This allows only a limited range of accommodation which amounts to 0.5 up to 2.5 D for a shift of 1 mm dependent on the power of the IOL optic. Therefore, accommodative IOLs with two lens optics designed to move in opposite directions have recently been developed. A shift of the IOL optic in a dual-optic accommodative IOL can effect about 2.5–3.0 D of accommodation (McLeod et al. 2003).

Deformable IOLs which can change their surface curvature like the natural human lens could theoretically reach an accommodative amplitude of 4–7 D (Ho et al. 2001).

Outcome

Results with accommodative IOLs so far have been mixed. Clinical results indicate better uncorrected visual acuity in near and intermediate distances and a higher percentage of subjective spectacle independence with single-optic accommodative than with standard monofocal IOLs. Movement of the IOL optic after topical application of pilocarpine was significantly higher in several accommodative IOL models than in standard IOLs. Other objective measurement methods, however, failed to discover significant differences in change of focus of the eye (Findl and Leydolt 2007).

The first results with double-optic accommodating IOLs showed a subjective accommodative amplitude of about 3.2 D. Movement of the IOL optics could be shown with dynamic ultrasound biomicroscopy (Ossma et al. 2007).

Complications

Complications of the accommodative IOLs can arise from the behavior of the implant inside the capsular bag. The moveable haptics have in some cases led to dislocations of the IOL optic. Because of the smaller optic diameter and the ability to move inside the capsule, the barrier effect of the sharp optic edge could be weakened with ensuing posterior capsule opacification.

In summary, accommodative IOLs can provide an improvement in intermediate and near vision while avoiding the optical side effects associated with multifocal IOLs. The predictability of the results is, however, still limited (Baumeister and Kohnen 2008).

Cross-References

- ▶ Accommodation, Cataract
- ▶ Ciliary body
- ▶ Intraocular lens
- ▶ Lens Epithelial Cells
- ▶ Presbyopia

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Accommodation, Cataract

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Definition

Accommodation is a dynamic change in the dioptric power of the eye which is executed in order to focus on targets in different distances.

Mechanism

The accommodative mechanism in its entirety was first described by Helmholtz in 1855. This description is in all relevant aspects still valid. The accommodative apparatus of the eye consists of the ciliary muscle, the zonular fibers forming the suspensory apparatus of the crystalline lens, and the lens itself. According to Helmholtz, during accommodation (focus change far–near) the tension of the zonular fibers which hold the lens in is far-accommodated state decreases as an effect of the contraction of the ciliary muscle and the resulting decrease in size of the ring formed by the ciliary muscle. As a result, the shape of the lens changes under the influence of the elastic lens capsule as it proceeds to its mechanical resting state. This causes an increase in lens curvature and anteroposterior lens thickness and a decrease of the equatorial lens diameter. These changes contribute to an increase in the overall dioptric power of the eye.

During the change in focus from near to far (disaccommodation) this process is reversed: by relaxation of the ciliary muscle and the elastic fibers of the choroid the diameter of the ciliary ring increases and the lens is pulled into its unaccommodated state by the zonular fibers. This results in decrease of anterior and posterior lens curvature and lens thickness and consecutively decrease of dioptric power of the eye so that the eye is focused on far objects.

Presbyopia

With advancing age, humans and many other species lose the ability to accommodate. This phenomenon, called presbyopia ("old-sightedness") is the most widespread visual impairment and affects everyone who advances into a sufficiently high age without exception. The decrease of accommodative amplitude begins at an age of 10–12 years and continues until the complete loss of the ability to accommodate at about 50–55 years of age. Presbyopia has been attributed to hardening of the lens, changes in lens and zonular geometry, as well as aging of the ciliary muscle (Glasser et al. 2003).

References

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Accommodation, Functional (Nonorganic/Nonphysiologic) Disorders of

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Synonyms

Accommodative excess; Accommodative spasm; Ciliary spasm; Focusing spasm; Spasm of accommodation

Definition

Accommodation is the adjustment of the eye for seeing objects at various distances accomplished by the ciliary muscle, which controls the lens of the eye and allows it to flatten or thicken, bringing images of objects into focus on the retina as needed. The circular ciliary muscle fibers affect the zonular fibers of the crystalline lens during accommodation.

When the ciliary muscle contracts, this releases tension on the lens caused by the zonules and causes the lens to become more spherical, adapting to shorter near range of focus. Accommodative spasm can result in ciliary muscle contraction and can be worsened by fatigue and strain.

Etiology

Functional accommodative disorders may be caused by trauma, eye-strain, or be nonorganic. Rarely true accommodative spasm can be organic.

Clinical Presentation

Functional accommodative disorders are characterized by intermittent attacks of accommodation, convergence, and miosis. Patients present with diplopia, from convergence spasm variable esotropia, blurred vision, miosis, pseudomyopia, headache, and facial pain localized in the eyes and may rarely complain of macropsia (in which the objects appear larger than their actual size). A characteristic of the blurred vision associated with this disorder is that it is often variable and worse toward the end of the day or after extensive near work.

Diagnostics

Patients may be diagnosed clinically by observation of the concomitant variable esotropia along with miosis that generally resolves when either eye is occluded with a patch. Clinical clues for diagnosis also includes bilateral variable abduction weakness with both eyes open but full abduction in each eye when opposite eye is patched and ductions are directly tested. Finally, retinoscopy and refraction with and without cycloplegia which establishes the presence of pseudomyopia.

Differential Diagnosis

Bilateral sixth nerve palsy, convergence excess, accommodative insufficiency, and esophoria.

Therapy

Functional accommodative spasm usually resolves spontaneously over time, and patients only require reassurance, typically. Psychiatric counseling may rarely be appropriate depending on etiology. With severe symptoms, treatment involves inhibiting the excessive accommodative tone with cycloplegic eye drops.

Cross-References

▶ Focusing Spasm
▶ Spasm of Accommodation

Further Reading

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Accommodative Excess

▶ Accommodation, Functional (Nonorganic/ Nonphysiologic) Disorders of

Accommodative Intraocular Lens

▶ Accommodating Intraocular Lens

Accommodative Micropsia

▶ Micropsia

Accommodative Spasm

▶ Accommodation, Functional (Nonorganic/ Nonphysiologic) Disorders of

Acetazolamide for Pseudotumor Cerebri

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Synonyms

Diamox

Definition and Medical Uses

Carbonic anhydrase inhibitor often used in treatment of glaucoma, altitude sickness, and epileptic seizures are the main story for the treatment of pseudotumour cerebri (idiopathic intracranial hypertension).

Use and Dose in Pseudotumor Cerebri

Carbonic anhydrase inhibitors are a first-line treatment and are believed to reduce the level of cerebrospinal fluid production as the mechanism at decreased intracranial pressure. A large multicenter trial, the idiopathic intracranial hypertension trial (IIHT), has supported the use of diet and acetazolamide in IIH. In adult patients, 500 mg twice per day is typically prescribed and advanced as required and tolerated by the patient. In young children, the recommended starting dose is typically 15 mg/kg per day up to 25 mg/kg per day with a maximum dose of 100 mg/kg per day or 2 g per day, but these higher doses are often not tolerated well.

Contraindication

Hyperchloremic acidosis, hypokalemia, hyponatremia, impaired kidney function, hypersensitivity to acetazolamide or less convincingly sulfonamides, and impairment of liver function are potential contraindications to the use of acetazolamide.

Adverse Reactions

The most common adverse effects are a metallic taste in the mouth particularly for carbonated beverages and peripheral paresthesias typically described as tingling in the hands and feet. These are generally however not dose-limiting side effects. Dizziness, light-headedness, increased urination, blurred vision, dry mouth, drowsiness, gastrointestinal upset, perioral and digital tingling, loss of appetite, metabolic acidosis, electrolyte imbalance, and nephrocalcinosis are less common. Rarely acetazolamide may cause potentially life-threatening anaphylactic reactions, Stevens-Johnson syndrome, or aplastic anemia.

Interactions

Acetazolamide increases the alkalinity of the urine and therefore can decrease excretion of other drugs (e.g., dextroamphetamine, anticholinergics, ephedrine, mexiletine, or quinidine). Increased urine alkalinity may also inhibit the conversion of methenamine to its active form formaldehyde. Acetazolamide can also potentiate salicylate toxicity by causing metabolic acidosis and enhancing the penetration of salicylate into tissues.

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Acetylsalicylic Acid

► Aspirin (for Carotid Artery Disease)

Achromatic Vision

► Achromatopsia Cerebral

Achromatopsia

► Red-Green Color Vision, Defects

Achromatopsia (Rod Monochromatism), Gene Defects Causing

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Synonyms

Rod monochromacy; Total color blindness

Definition

Autosomal recessive, congenital retinal disease characterized by severely reduced or completely absent color vision, photophobia, nystagmus, reduced visual acuity, and nondetectable cone electroretinograms.

Etiology

Congenital achromatopsia is caused by a disruption in the cone phototransduction cascade. Mutations in the genes encoding the α and β subunits of the cone cyclic nucleotide-gated channel (CNGA3 & CNGB3, respectively), the α subunit of cone transducin (GNAT2), and phosphodiesterase 6C (PDE6C) have been associated with the disease. Over 115 different mutations have been reported. These genes are expressed exclusively in the cone photoreceptor defects in them, which impair the cones' ability to hyperpolarize in response to light. There is phenotypic variability depending on the genotype, with novel high-resolution imaging tools being used to define the retinal phenotype on a cellular level.

Clinical Presentation

Individuals with rod monochromacy first present early in childhood with photophobia and nystagmus. Visual acuity is reduced (20/100–20/600) and visual fields may be normal or slightly constricted. Retina is normal in appearance on funduscopic examination. Retinal thinning in the macula may be present on optical coherence tomography. Eccentric fixation is also common. On the electroretinogram, cone (photopic) response is absent or significantly reduced while the rod (scotopic) response is normal or only mildly depressed.

Diagnosis

Clinical observation, electroretinography, and color vision testing are mandatory. Dark adaptometry, if available, can provide definitive diagnostic data. Pseudoisochromatic plates are of little value; rather color matching performance on an anomaloscope must be assessed. Fluorescein angiography and electroretinography can help differentiate these patients from those with cone or cone-rod dystrophies. Genetic testing should be considered, as mutations in *CNGA3*, *CNGB3*, *PDE6C*, and *GNAT2* have been associated with the disorder.

Differential Diagnosis

Differential diagnosis includes blue-cone monochromacy, cone monochromatism, cone dystrophies, and cerebral achromatopsia.

Therapy

Treatment of achromatopsia may include dark or special filter glasses or red-tinted contact lenses to reduce photophobia and potentially improve visual acuity, low vision aids (high-powered magnifiers), and occupational aids. Gene therapy has been used to restore cone function in mouse & dog models of the disease. Human trials are currently in preplanning stages.

Prognosis

Typically, congenital achromatopsia is a stationary condition.

Epidemiology

1:30,000, equal incidence in males and females.

Cross-References

- ▶ Achromatopsia
- ▶ Cerebral Achromatopsia
- ▶ Color Blindness
- ▶ Color Vision, Three Cone Opsins
- ▶ Cone Dystrophies/Degeneration
- ▶ Cone-Rod Dystrophy
- ▶ Inherited Color Vision Defects
- ▶ Legal Blindness: Definition
- ▶ Photophobia
- ▶ Phototransduction Cone/Rod

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Achromatopsia Cerebral

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Synonyms

Achromatic vision; Color blindness; Color vision deficiency; Daltonism; Dichromatic vision

Definition

Cerebral achromatopsia is a form of color blindness that results from cortical damage. It is characterized by severe or total color vision deficits. This loss may be complete or partial, and it may or may not be accompanied by other visual defects.

Etiology

Cerebral achromatopsia in contrast to retinal etiologies is due to brain disease. It can arise after meningitis, trauma, tumor, inflammation, or cerebral infarction. The underlying structural etiologies typically involve the lingual and fusiform gyri in the ventromedial aspect of the occipital lobe. Bilateral lesions are usually necessary for complete cerebral achromatopsia. Because the lingual and fusiform gyri border the lower lip of the calcarine sulcus, the homonymous hemianopsia when present typically involves the upper visual fields. If the lesion is more extensive and involves the upper lip of the calcarine sulcus, the scotoma will involve the lower visual fields as well. If the lesion is more widespread anteriorly within the fusiform gyrus, it may also lead to a prosopagnosia.

Clinical Presentation

Patients complain of monochromatic or washed out vision with or without the homonymous hemianopsia or cortical visual impairment.

Diagnostics

Diagnosis is based on medical history, color vision testing, electrophysiology, visual fields, psychophysical tests, and optical coherence tomography. Color vision tests include chairside testing (e.g., Ishihara or HRR color plates) or more extensive testing (e.g., the Farnsworth-Munsell 100-Hue Test, the Farnsworth D-15).

Differential Diagnosis

Congenital achromatopsia
Acquired retinopathy or optic neuropathy

Therapy

Treatment should be directed at the underlying etiology.

Cross-References

- ▶ Dyschromatopsia
- ▶ Lanthony Tritan Album
- ▶ Lanthony Tritan Plates, in Color Vision Evaluation
- ▶ Red-Green Color Vision, Defects

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Acne Rosacea

- ▶ Rosacea: Overview

Acquired Melanocytic Nevus

- ▶ Compound Nevus
- ▶ Nevus, Intradermal
- ▶ Nevus, Junctional

Acquired Sessile Hemangioma

- ▶ Vascular Tumors Disease of the Conjunctiva

Acrocephalopolysyndactyly Type II

- ▶ Carpenter Syndrome

Acrochordon

- ▶ Squamous Cell Papillomas of Eyelid

Acrylic Intraocular Lens

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Synonyms

Acrylic IOL; Polyacrylic IOL

Definition

Artificial lens made of transparent acrylic that is implanted in the eye and performs in focusing images. An acrylate polymer belongs to a group of polymers which could be referred to generally as plastics. They are noted for their transparency and resistance to breakage and elasticity.

Epidemiology

According to industry data worldwide, a number of implanted IOLs are estimated at between 6 and 10 million a year. Most of these IOLs are made of acrylic.

History

In 1949, Sir Harold Ridley implanted the first IOL in a human eye at St. Thomas' Hospital in London, UK. This was performed as an extracapsular surgery with a large incision size. With the development of phacoemulsification and smaller-incision surgery, the search for new foldable IOL materials led to the exploration of poly-hydroxyethyl methacrylic acid (poly-HEMA). In the 1980s, G.D. Barret developed the first hydrogel IOL (IOGEL PC-12), which was implanted in 1983 in Perth, Australia. These hydrogels were soft hydrophilic materials. Later on, hydrophobic acrylic IOLs were developed which represent the most common implanted foldable IOL today (Barrett et al. 1986; Kohnen and Koch 2009; Werner 2008).

Clinical Features

There are two different basic types of acrylic IOL:

- Hydrophilic
- Hydrophobic

The differences between these types are displayed in the entries "Hydrophilic acrylic intraocular lens" and "Hydrophobic acrylic intraocular lens"

Tests

During the decades, acrylic IOLs have undergone extensive research and testing in Europe, Asia, and the United States and have been proven safe for the treatment of cataracts and refractive errors.

Differential Diagnosis

See entries "▶ Hydrophilic" and "▶ Hydrophobic Acrylic Intraocular Lens."

Etiology

The term acrylic refers to the Latin word "acer" or Greek word "ákros" that means "sharp" due to the smell of acrylic acid.

Treatment

See also entries: "▶ Cataract Surgery" and "▶ Refractive Surgery" describing different IOL implantation techniques.

Cross-References

- ▶ Cataract Surgery
- ▶ Foldable Intraocular Lens
- ▶ Hydrophilic
- ▶ Hydrophilic Acrylic Intraocular Lens
- ▶ Hydrophobic
- ▶ Hydrophobic Acrylic Intraocular Lens
- ▶ Intraocular Lens

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Acrylic IOL

- ▶ Acrylic Intraocular Lens

Actinic (Solar) Keratosis

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Synonyms

Senile keratosis; Solar keratoses

Definition

A premalignant cutaneous lesion (precursor form of cutaneous squamous cell carcinoma).

Basic Characteristics

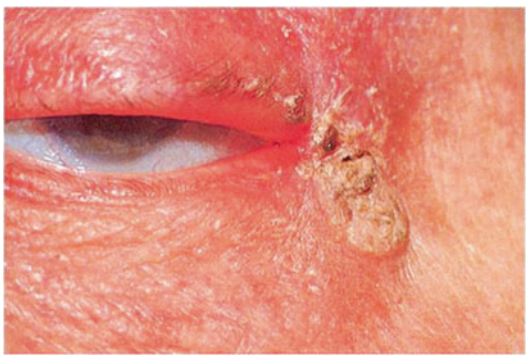
Actinic keratosis typically occurs in fair-skinned individuals, especially in the elderly, and affects face, hands, bald scalp, and eyelids (areas with chronic ultraviolet exposure). Individuals who are immunosuppressed are also at higher risk.

Some authors consider these lesions to be precancerous and others consider them to be a squamous cell carcinoma confined to the lower portion of the epidermis (incipient intraepidermal squamous cell carcinoma) (Albert and Jakobiec 2008; Shields and Shields 2008).

Usually it presents as multiple, erythematous, scaly plaques on sun-exposed skin (Fig. 1). They may range from millimeters up to 1 cm in size. Frequently keratosis, or an elevated white flaky crust, is seen on the surface and a nodular, horny, or warty configuration can be present.

A skin biopsy is indicated to confirm the diagnosis and to rule out invasive squamous cell carcinoma. Therefore, biopsies of suspected actinic keratosis should include the base of the lesion.

Treatment alternatives include surgical destruction and medical therapy. Excision, cryotherapy, curettage and electrosurgery, and laser surgery (CO_2 laser) are among surgical modalities. Medical therapy comprise fluorouracil (5-FU), imiquimod cream, topical diclofenac gel, photodynamic therapy (PDT), and chemical peeling. On the eyelid, these topical agents are not



Actinic (Solar) Keratosis, Fig. 1 Actinic ketatosis showing white scales near the medial canthus

usually applied because they can produce an intense inflammatory reaction and damage to the ocular surface (Albert and Jakobiec 2008; Shields and Shields 2008).

The prognosis is good, but early treatment should occur before the lesion develops into skin cancer (▶ squamous cell carcinoma). Follow-up of these lesions is necessary.

Cross-References

- ▶ Basal Cell Carcinoma of Eyelid
- ▶ Bowen's Disease
- ▶ Melanomas, Conjunctival
- ▶ Seborrheic Keratosis
- ▶ Squamous Cell Carcinoma, of the Conjunctiva

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Actinic Cheilitis (AK on the Lips)

▶ Actinic Keratosis

Actinic Keratosis

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Synonyms

Actinic cheilitis (AK on the lips); Senile hyperkeratosis; Senile keratosis; Solar keratosis

Definition

Actinic keratosis (AK) is a common skin lesion usually presenting as small, rough, scaly erythematous macules or papules on sun-exposed parts of the body. It is a precursor form of squamous cell carcinoma.

Etiology

AKs are caused by cumulative UV exposure, most commonly in the form of sunlight. UV rays induce mutation of the tumor-suppressor gene P53, and subsequent proliferation of the mutated atypical epidermal keratinocytes can develop into AK.

Clinical Presentation

AKs are small (usually 0.2–0.6 cm) and range in color from flesh colored or pink to slightly hyperpigmented (yellow brown). They are found frequently with a superimposed scale or hyperkeratosis that is rough upon touch and tender for the individual. AKs are found on sun-exposed parts of the body, commonly the face, forearms, dorsum of hands, eyelids, lower legs, and the balding scalp and tops of the ears. Multiple clinical and subclinical lesions may present in an area of sun-damaged skin, a concept known as "field cancerization."

Diagnosis

AKs that appear premalignant may be diagnosed by observation and palpation. A skin biopsy including the base of the lesion is recommended to confirm the diagnosis and to rule out invasive squamous or basal cell carcinoma.

Microscopy of AK lesions reveals atypical aggregates and pleomorphic keratinocytes in the basal cell layer that may extend to granular and cornified layers. Abnormal keratinocytes may cause parakeratosis of the overlying stratum corneum, leading to the signature "flag sign" of visible alternating orthohyperkeratosis above the spared epithelium.

A distinct margin also appears between the normal epidermis and the area of AK at lateral edges.

Differential Diagnosis

Squamous cell or basal cell carcinoma
Bowen disease
Seborrheic keratosis
Solar lentigines
Lentigo maligna
Nummular eczema
Lichenoid keratosis
Cutaneous lupus

Prophylaxis

Sunscreen applied properly and daily may protect against development of AK.

Therapy

Treatment options include surgical destruction and medical therapy.

Cryosurgery, excision, curettage, electrosurgery, and laser surgery (CO_2 laser) are possible surgical alternatives. Cryosurgery with liquid nitrogen is the most common method of treatment. It may be particularly superior for thicker lesions, but may leave scars.

Medical therapies include topical solutions such as fluorouracil (5-FU), imiquimod cream, or diclofenac gel, as well as chemical peeling or photodynamic therapy (PDT) with aminolevulinic acid and blue light. Transplant patients on immunosuppression therapy must take caution in using imiquimod cream due to its immunostimulatory properties. Routine follow-up skin examinations are necessary.

Prognosis

Prognosis of treated AK is excellent, if the lesion is treated early before developing into squamous cell carcinoma.

Epidemiology

AKs are so common that they account for more than 10% of visits to dermatologists. Individuals at higher risk of developing AKs include the elderly, those with lighter skin phototypes, and those with a history of chronic sun exposure.

Cross-References

- ▶ Bowen's Disease
- ▶ Conjunctival Squamous Cell Carcinoma
- ▶ Melanomas, Conjunctival
- ▶ Nevoid Basal Cell Carcinoma Syndrome
- ▶ Seborrheic Keratosis

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Acular

▶ Ketorolac Tromethamine

Acular LS

▶ Ketorolac Tromethamine

Acular PF

▶ Ketorolac Tromethamine

Acute Angle Closure

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Synonyms

Primary angle closure; Pupillary block

Definition

Acute apposition of the peripheral iris to the trabecular meshwork resulting in reduced drainage of aqueous humor leading to a rise of intraocular pressure.

Etiology

Narrow occludable angles, often in hyperopic eyes with smaller than average anterior segment dimensions.

Prophylaxis

Prophylactic iridotomy or iridectomy in the fellow eye of a patient who has suffered acute angle closure, or in eyes with an occludable angle in gonioscopy.

Clinical Presentation

Patients may be asymptomatic or present with a unilateral attack of decreased vision, blurring, and pain, often occurring during dim illumination. Occasionally patients will present with nausea and vomiting.

Diagnostics

An affected eye may show conjunctival hyperemia, corneal edema, shallow anterior chamber, and a mid-dilated pupil in a slit lamp examination. Tonometry will show a high intraocular pressure. Gonioscopic examination reveals angle closure with iridocorneal contact.

Therapy

The definite management of acute angle-closure glaucoma is breaking the relative pupillary block with a laser iridotomy or a peripheral iridectomy. Medical therapy to lower the intraocular pressure serves in order to relieve the symptoms and to enable iridotomy or iridectomy.

Prognosis

Variable from complete recovery without optical disk or visual field damage to profound glaucomatous vision loss, depending on duration of pupillary block and rise of intraocular pressure. Following an episode of symptomatic angle closure, reports suggest that satisfactory intraocular pressure control can be achieved in 42–72% of cases with pupillary block alone. Once primary angle-closure glaucoma, defined as structural damage to the disk and a field defect, has developed, most cases (94–100%) will require further treatment to control intraocular pressure.

Epidemiology

The prevalence of pupillary block ranges from 0.04% in Europe and Australia to 1.37% in Asia.

Cross-References

- ▶ Angle-Closure Glaucoma
- ▶ Intraocular Pressure
- ▶ Iridotomy

Further Reading

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Acute Angle Closure in Dislocated or Intumescent Lens

► Lens-Induced Angle-Closure Glaucoma

Acute Conjunctivitis

► Adenoviral Keratoconjunctivitis

Acute Contusion Glaucoma

► Traumatic Glaucoma

Acute Hemorrhagic Conjunctivitis

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Synonyms

Epidemic keratoconjunctivitis (EKC); Hemorrhagic viral keratoconjunctivitis

Definition

Self-limited, rapid onset viral conjunctivitis with subconjunctival hemorrhage

Etiology

Adenoviruses, *Enterovirus* type 70 (EV70), *Coxsackievirus* A type 24 variant (CA24v)

Clinical Presentation

Patients have subconjunctival hemorrhage that is either petechial or confluent. The latter can give a posttraumatic appearance. Hyperemia, papillary reaction, and follicles are generally noted in the palpebral conjunctiva. Some or all of the following may be present: rapid onset of eye discomfort, tearing, eyelid swelling, discharge, chemosis, preauricular adenopathy, superficial punctate keratitis, and photophobia. The discomfort is sometimes described as foreign body sensation. In rare cases, flare in the anterior chamber suggestive of mild iritis has been reported. Signs and symptoms can present in one eye or both. The condition can be part of a more generalized pharyngoconjunctival fever.

Diagnosis

Diagnosis is typically based on clinical findings. Immunochromatography and enzyme immunoassay can be done in 10 min and 70 min, respectively. The sensitivity of both tests is about 50% and the specificity is almost 100%. Polymerase chain reaction (PCR) can be used for identification and results are available within days. Cell culture isolation and the neutralization test (using antibody serum) are also options but can take weeks for results to become available.

Differential Diagnosis

Traumatic subconjunctival hemorrhage, herpes simplex virus, toxic conjunctivitis, Molluscum, pediculosis, gonococcus, bacterial conjunctivitis, allergic conjunctivitis, chlamydia

Therapy

This is a self-limited condition that typically resolves within 2 weeks, more or less. It is highly contagious and precautions should include handwashing and proper hygiene. Treatment is meant to address symptoms, e.g., artificial tears and cool compresses. If discharge is excessive or the condition becomes chronic, then conjunctival cultures are recommended to look for nonviral causes.

Prognosis

The disease often exhibits spontaneous resolution. A secondary bacterial infection is possible and should be treated accordingly.

Epidemiology

The condition was first reported in Ghana in 1969. The local population called it "Apollo" disease because it occurred around the same time as the Apollo mission's moon landing. Since then, outbreaks of AHC have been reported in both developing and developed countries, mostly in tropical and subtropical areas. Epidemics last several months and affected populations have been reported numbering 10,000–200,000.

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Acute Hydrops Keratoconus

► Hydrops, Keratoconus

Acute Idiopathic Blind Spot Enlargement

► Acute Idiopathic Enlargement of Blind Spot

Acute Idiopathic Enlargement of Blind Spot

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Synonyms

Acute idiopathic blind spot enlargement

Definition

Symptomatic enlargement of the blind spot without commensurate optic disk edema, occurring in conjunction with presumed disease of the peripapillary retina (e.g., papilledma).

Etiology

This disorder may be triggered by a prodromal viral illness.

Clinical Presentation

Patients present with variable features including normal or decreased visual acuity, photopsia, and

abrupt onset of visual field defects (i.e., enlarged blind spot). Patients may present with a relative afferent pupillary defect. The most common presentation is in a young myopic female. The retina and optic nerve are normal initially but may show peripapillary retinal pigment epithelial changes later.

Diagnostics

Diagnosis is based on medical history, vision testing, visual field testing, fundoscopic exam, fluorescein angiography, optical coherence tomography (OCT) of the retina, or focal or multifocal electroretinography. Visual field testing shows enlarged blind spots, highly variable in terms of size, but which typically have steep margins. Fundoscopic exam is usually normal. Fluorescein angiography may show peripapillary hyperfluorescence from late RPE staining. Later fundus changes may occur, however multifocal electroretinography (MERG) might show depressed wave forms in the peripapillary retina.

Differential Diagnosis

Multiple evanescent white dot syndrome, acute zonal occult outer retinopathy, optic neuritis, migraine, papilledema, chiasmal lesion, optic nerve drusen, anterior ischemic optic neuropathy, benign intracranial hypertension, peripapillary coloboma, glaucoma, retrobulbar mass, inverted disk, juxtapapillary choroiditis, progressive myopia with a temporal crescent, inferior conus, adverse side effects of systemic drugs.

Therapy

No current treatment is known for this disorder.

Prognosis

Patients typically show spontaneous improvement of the enlarged blind spot within 3 months, but some patients have permanent visual symptoms.

Further Reading

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Acute Multifocal Placoid Pigment Epitheliopathy

▶ Pigment Epitheliopathy

Acute Posterior Multifocal Placoid Pigment Epitheliopathy

▶ Pigment Epitheliopathy

Acute Retinal Necrosis (Necrotizing Herpetic Retinitis)

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Synonyms

Necrotizing viral retinitis

Definition

Necrotizing peripheral vaso-occlusive retinitis

Etiology

A rare, aggressive, and potentially devastating syndrome associated with human herpes viruses. The most common cause is varicella-zoster virus

(VZV), followed by herpes simplex virus (HSV-1, HSV-2), and rarely by cytomegalovirus (CMV) and Epstein-Barr virus. It usually occurs in healthy immunocompetent patients; however, HSV-1 acute retinal necrosis (ARN) was reported in patients with past or concurrent herpes encephalitis, and VZV and HSV-2 ARN were related to meningitis. Association between ARN and HLA-DQw7 (phenotype Bw62) and DR4 was found in Caucasian patients in the USA and with HLA-Aw33, HLA-B44, and HLA-DRw6 antigens in patients in Japan, suggesting a possible genetic contribution in some patients (Bodaghi and LeHoang 2009; Whitcup 2010).

Clinical Presentation

ARN was first described in 1971 by Akira Urayama and colleagues as a clinical syndrome consisting of acute unilateral panuveitis associated with retinal periarteritis progressing to diffuse necrotizing retinitis and, ultimately, rhegmatogenous retinal detachment. The authors suggested the term Kirisawa–Urayama uveitis in honor of their teacher Professor Naganori Kirisawa, who was then Professor of Ophthalmology at Tohoku University. The term "BARN," for bilateral ARN, was coined by Young and Bird in 1978. In 1994, the Executive Committee of the American Uveitis Society refined the definition of ARN based on clinical characteristics and disease course.

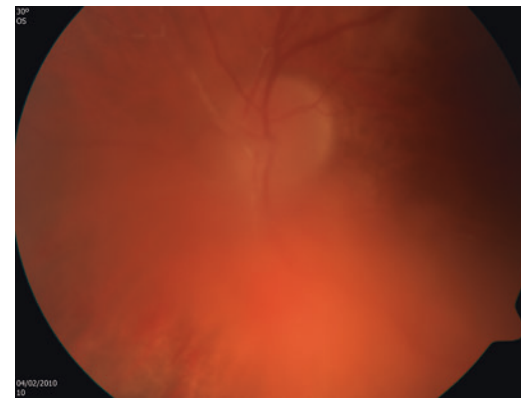
The most common complaints at presentation are red eye, blurred vision, photophobia, and ocular pain. Ocular examination findings may include episcleritis, scleritis, keratitis, and/or anterior chamber inflammation, which may be either non-granulomatous or granulomatous. Posterior segment findings include vitreous inflammation, patchy full-thickness necrotizing retinitis which may present as either confluent or multifocal patches of retinitis involving the peripheral retina, occlusive periarteritis and in some cases optic disk involvement may be seen.

The clinical diagnosis of ARN is based on the diagnostic criteria established by the American Uveitis Society, which consists of: (1) one or more discrete foci of peripheral retinal necrosis, (2) occlusive retinal vasculitis with arteriolar involvement, (3) prominent inflammation in the anterior and posterior chambers, (4) circumferential disease spread, and (5) rapid progression of disease in the absence of treatment.

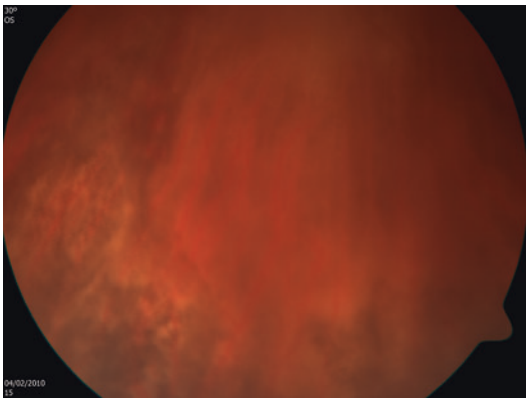
With prompt initiation of treatment, progression of the retinitis can usually be halted within 2–4 weeks. As the active retinal infection and inflammation resolve, affected areas develop pigmentary changes, retinal thinning, and atrophy, often producing a scalloped appearance at the junction of the involved and uninvolved retina. Vitreous organization and traction may progress during this phase, producing retinal breaks, retinal detachment, and proliferative vitreoretinopathy. Delayed complications of ARN may include chronic vitritis, macular edema, optic atrophy, epiretinal membrane formation, viral relapse with cessation of antiviral medication, and phthisis (Bodaghi and LeHoang 2009; Whitcup 2010).

Diagnostics

The diagnosis is based on clinical features of the disease and confirmed by demonstration of herpetic viral DNA in aqueous or vitreous samples by polymerase chain reaction (PCR) (Figs. 1 and 2) (Bodaghi and LeHoang 2009; Whitcup 2010).



Acute Retinal Necrosis (Necrotizing Herpetic Retinitis), Fig. 1 LE- inferior-nasal peripheral retinal necrosis with occlusive arterial vasculitis and severe vitritis, in a patient with a past history of HSV-1 encephalitis and a positive HSV-1 PCR result from vitreous sample



Acute Retinal Necrosis (Necrotizing Herpetic Retinitis), Fig. 2 LE- inferior-nasal peripheral retinal necrosis with occlusive arterial vasculitis and severe vitritis, in a patient with a past history of HSV-1 encephalitis and a positive HSV-1 PCR result from vitreous sample

Differential Diagnosis

- Cytomegalovirus retinitis may present similarly but be distinguished by mild inflammatory findings in the anterior chamber and vitreous, scattered hemorrhages, or granular lesions, and patients are often in an immunosuppressed state.
- Progressive outer retinal necrosis occurs in immunocompromised patients and characterized by extensive, rapidly progressing full-thickness necrosis of the retina involving initially the posterior pole, with little or no inflammatory component and spares the retinal vasculature.
- Other noninfectious diseases as Behcet's disease and intraocular tumors can present with retinitis that mimics ARN (Bodaghi and LeHoang 2009; Whitcup 2010).
- Nonviral infectious agents as *Toxoplasma gondii*, bacteria, or fungi.

Prophylaxis

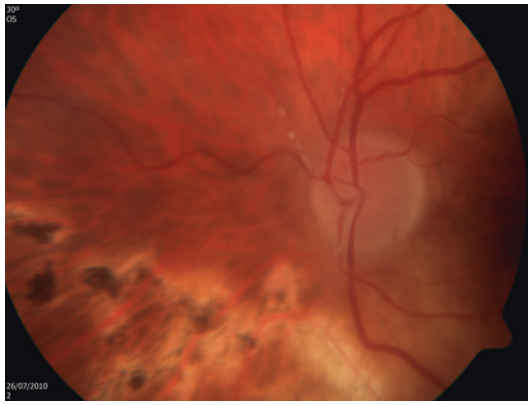
- Long-term antiviral therapy is the only possible way to avoid relapses.
- Prophylactic laser barricade applied posteriorly to necrotic areas has been suggested to reduce incidence of secondary retinal detachment.
- Early vitrectomy with intravitreal acyclovir lavage in addition to standard therapy has been suggested to reduce the rate of rhegmatogenous retinal detachment (Bodaghi and LeHoang 2009; Whitcup 2010; Wong et al. 2013).

Therapy

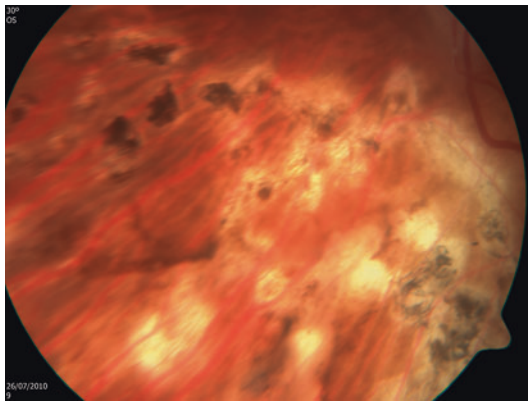
- The classical approach includes systemic intravenous acyclovir 10 mg/kg three times per day for 7–14 days, continued by oral acyclovir 800 mg five times a day for VZV-related ARN, or 400 mg five times a day for HSV-related ARN, for at least 6 weeks.
- An alternative treatment includes oral valacyclovir of 1 or 2 g three times per day for at least 6 weeks.
- For CMV-related ARN, an oral treatment with valganciclovir 900 mg twice per day for 3 weeks' induction and then 450 mg twice per day for maintenance. (In HIV patients prolonged therapy/prophylaxis until the CD4 count is repeated above 100 cells/μl for at least 6 months.)
- Oral corticosteroids (0.5–1 mg/kg/day), tapered along the course of antiviral therapy, are given in cases of significant inflammation or macula/optic nerve involvement (Figs. 3, 4, and 5).
- Intravitreal injections with ganciclovir (2 mg/0.1 ml) or foscarnet (2.4 mg/0.1 ml) may be given in patients resistant to or have contraindications to conventional therapy or as adjunctive with systemic treatment.
- Vitrectomy is done for rhegmatogenous retinal detachment, or in cases with poorly or non-responsive progressive retinal lesions and severe inflammation. Pars plana vitrectomy with endolaser and silicone oil tamponade has shown success in retinal reattachment and vision improvement (Bodaghi and LeHoang 2009; Whitcup 2010; Wong et al. 2013).

Prognosis

Visual prognosis depends mainly on the duration from disease onset to treatment.

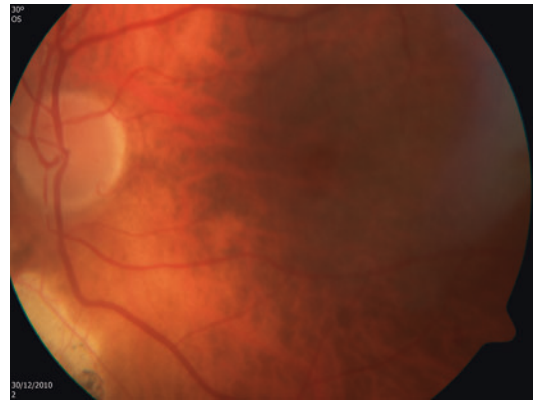


Acute Retinal Necrosis (Necrotizing Herpetic Retinitis), Fig. 3 LE- Post-systemic antiviral and corticosteroids treatment with application of laser photocoagulation posteriorly to necrotic areas. Vitritis and retinitis resolved and the macula is spared



Acute Retinal Necrosis (Necrotizing Herpetic Retinitis), Fig. 4 LE- Post-systemic antiviral and corticosteroids treatment with application of laser photocoagulation posteriorly to necrotic areas. Vitritis and retinitis resolved and the macula is spared

Generally, VZV–ARN patients tend to have more severe disease than HSV-ARN patients and often result in poorer visual prognosis. The onset of ARN syndrome is generally unilateral with contralateral eye involvement in approximately 2/3 of the cases, usually within 1–6 weeks from disease onset. Adequate antiviral therapy showed to reduce fellow-eye involvement to approximately 9%. Retinal detachment may develop in up to 75% of untreated infected eyes, but with proper treatment



Acute Retinal Necrosis (Necrotizing Herpetic Retinitis), Fig. 5 LE- Post-systemic antiviral and corticosteroids treatment with application of laser photocoagulation posteriorly to necrotic areas. Vitritis and retinitis resolved and the macula is spared

incidence is reduced to 20–52% of the cases (Bodaghi and LeHoang 2009; Whitcup 2010).

Epidemiology

ARN syndrome is rare; it was diagnosed in only 1.3% of 3,060 endogenous uveitis patients in Japan, and two national population-based studies in the United Kingdom reported its incidence to be approximately one case per 1.6–2.0 million population per year. There is no known association between gender, race or age, and the incidence of ARN. The mean onset age reported is in ascending order of HSV-2, HSV-1, and VZV–ARN syndrome (Bodaghi and LeHoang 2009; Whitcup 2010).

Cross-References

▶ Cytomegaloviruses, Retinitis

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Acute Zonal Occult Outer Retinopathy (AZOOR)

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Acute zonal occult outer retinopathy (AZOOR), initially described by Gass during the Donders' Lecture in 1993 (Gass 1993), is a syndrome characterized by sudden unilateral or bilateral zonal loss of outer retinal function corresponding to visual field defects, photopsias, variable or limited funduscopic changes, and electroretinogram (ERG) abnormalities. Vitreous inflammation can develop in those eyes that suffer higher degrees of visual field loss, and involvement of the fellow eye can occur weeks or even several years after initial presentation. Affected patients occasionally complain of an antecedent viral illness and their symptoms persist for approximately 4–6 months, after which the visual field loss often stabilizes or slightly improves (Gass et al. 2002). Late recurrences and progression have been described in some patients (Gass et al. 2002).

Since its initial description, features of AZOOR have been described in patients with multifocal choroiditis and panuveitis (MFC), punctate inner choroidopathy (PIC), multiple evanescent white dot syndrome (MEWDS), acute idiopathic blind spot enlargement syndrome (AIBSE), and acute macular neuroretinopathy (AMN), thus expanding the clinical spectrum of the syndrome to what Gass termed as AZOOR complex disorders (Gass et al. 2002; Gass 2003; Jampol and Wiredu 1995). Due to the variable presentation of AZOOR, its diagnosis can be confused with optic neuropathy and paraneoplastic, toxic, and autoimmune retinopathy. However, with the advent of new imaging modalities such as spectral-domain optical coherence tomography (SD-OCT) and fundus autofluorescence (FAF), our understanding of AZOOR has significantly expanded, thus improving diagnostic accuracy and analysis of treatment response.

Clinical Presentation

Most patients with AZOOR are young or middle-aged adults, myopic, generally healthy, and predominantly female. Compared to the general population, they or their first-degree relatives have a higher incidence of autoimmune disease(s) (Gass et al. 2002). AZOOR patients typically present with acute scotoma and photopsias corresponding to the zone of field loss. The photopsias can predate the scotoma or begin simultaneously with the field loss. They are more noticeable in bright lighting and daylight, in contrast to photopsias from vitreous degeneration, which are typically short lived and identified in dim lighting or at nighttime. Those patients with disabling photopsias sometimes present to the clinic wearing sunglasses. Photopsias are variably described as "fireworks, heat waves emanating from the road, microbes moving under a microscope, or moving colorful lights" (Gass 1993; Gass et al. 2002). Chronic photopsias can develop in patients who develop permanent fundus changes as a result of chronic photoreceptor destruction. During the evaluation, some patients complain of an antecedent viral illness or migraine type headaches prior to the onset of visual symptoms. On exam, those patients with larger scotomas or greater photoreceptor involvement can have vitreous cells. A small percentage of patients can have perivenous exudation or sheathing; however, a normal clinical exam is typical. Prior to accurate diagnosis of the condition, several patients undergo evaluation for functional vision loss or for neurological etiologies to explain the field loss.

Fundus Examination

The clinical spectrum of AZOOR is variable and can be unilateral or bilateral at initial presentation. Patients with bilateral involvement can have asymmetric clinical findings between eyes (Fig. 1). Fundus examination can reveal either a normal exam (Fig. 2a, b) suggesting an occult manifestation or demonstrate peripapillary, segmental, or diffuse pigment changes, representing overt manifestation of the syndrome. Some patients develop a yellow ring defining the border of the zone of involvement of the photoreceptors. A subset of patients can present with a gray-white ring demarcating the zone of visual field loss, which has been described as acute annular outer retinopathy (AAOR) and is likely a variant of AZOOR. Therefore, an eye with AZOOR can demonstrate a wide spectrum of fundus findings, which requires further testing including visual fields, fluorescein angiography (FA), FAF, SD-OCT, and ERG in making the diagnosis.

Visual Field

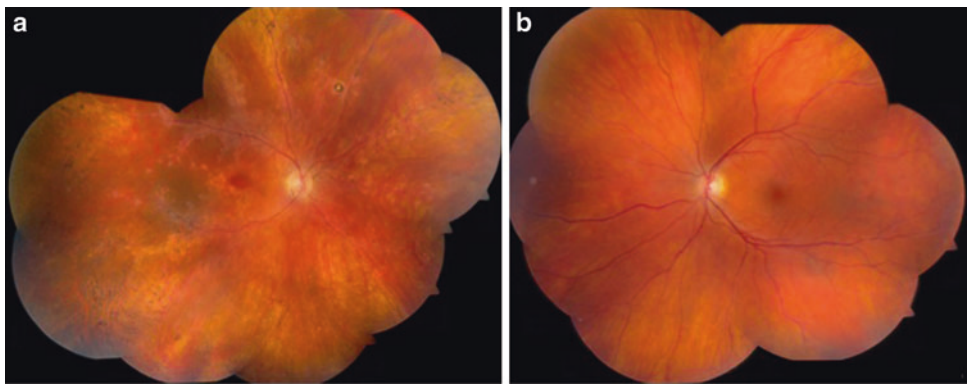
Visual field changes correspond to regions of photoreceptor involvement in AZOOR. Therefore, Goldmann visual field testing, which evaluates the entire visual field, is especially useful to confirm a diagnosis. Visual field changes are variable depending on where in the retina the photoreceptors are affected. The majority of cases involve the peripapillary region, which results in an enlarged blind spot or a scotoma emanating from the normal blind spot on visual field testing (Fig. 3a, b). Otherwise, the field loss can be peripheral or multifocal (Fig. 3c). Over time, the field loss can stabilize and even improve in a small subset of patients that are diagnosed in early stages of the disease and treated with corticosteroids and oral antiviral medications (Fig. 4). Therefore, follow-up visual field testing is beneficial for monitoring disease progression or stabilization.

Fluorescein Angiography

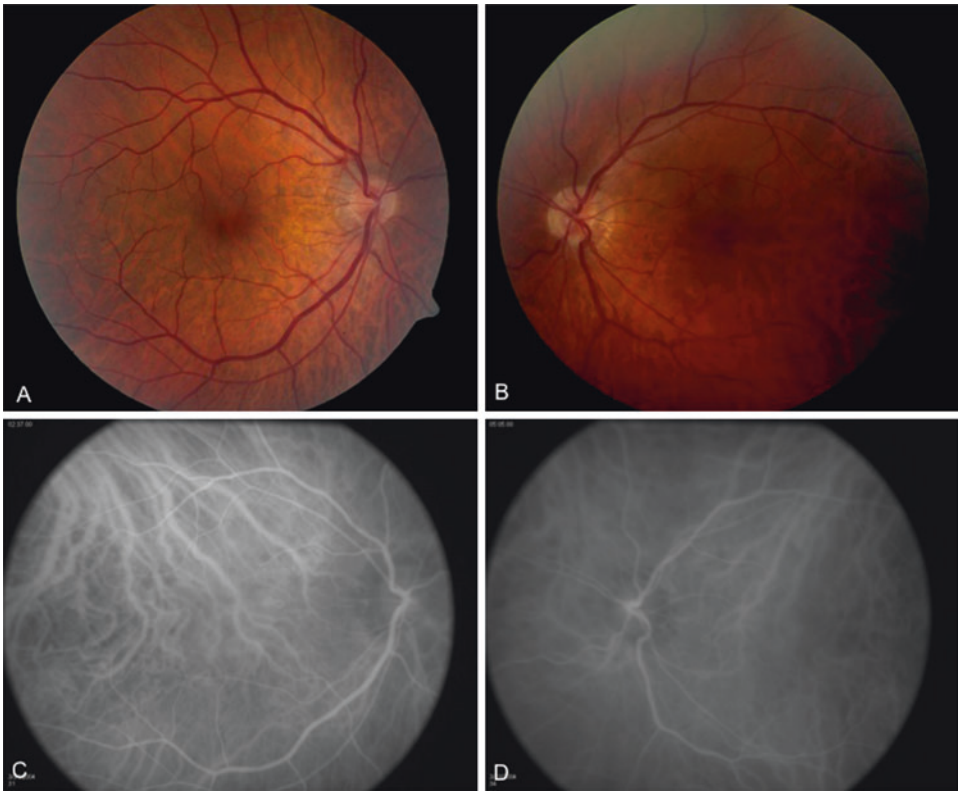
Fluorescein angiogram findings are generally normal in patients with early symptoms and minimal to no funduscopic changes (Figs. 5c and 7c). However, in chronic and more advanced cases, photoreceptor cell death can occur, which results in pigmentary changes at the level of the retinal pigment epithelium (RPE). This can result in RPE migration and a bone spicule appearance similar to retinitis pigmentosa in the later course of disease in some eyes. Angiography at this stage would reveal hyperfluorescence from window defects created by the zones of RPE degeneration (Figs. 6c, d and 7d).

Indocyanine Green Angiography

Indocyanine green angiography (ICG) findings have not been studied extensively in AZOOR. However, occult cases generally have normal



Acute Zonal Occult Outer Retinopathy (AZOOR), Fig. 1 Montage color fundus photographs of a patient with bilateral asymmetric AZOOR and an interval of 8 years between disease onset in the right eye versus left eye. (**a**) Right eye photos revealing diffuse atrophy and pigmentary changes and (**b**) left eye without significant fundus abnormalities despite symptoms of temporal field defect that progressed over 4 months and stabilized on immunosuppressive therapy



Acute Zonal Occult Outer Retinopathy (AZOOR), Fig. 2 Color fundus photographs of a patient with bilateral occult AZOOR with large temporal field defects in each eye, right eye affected 10 years prior to left. (**a**) Right and (**b**) left eyes demonstrate normal fundus appearance. ICG of (**c**) right and (**d**) left eyes reveals no abnormalities

ICG findings (Fig. 2c, d). In addition, late stage AZOOR lesions with pigment alterations and zones of RPE loss have shown hypofluorescence on ICG as a result of choriocapillaris atrophy within the corresponding region (Mrejen et al. 2014; Spaide 2004).

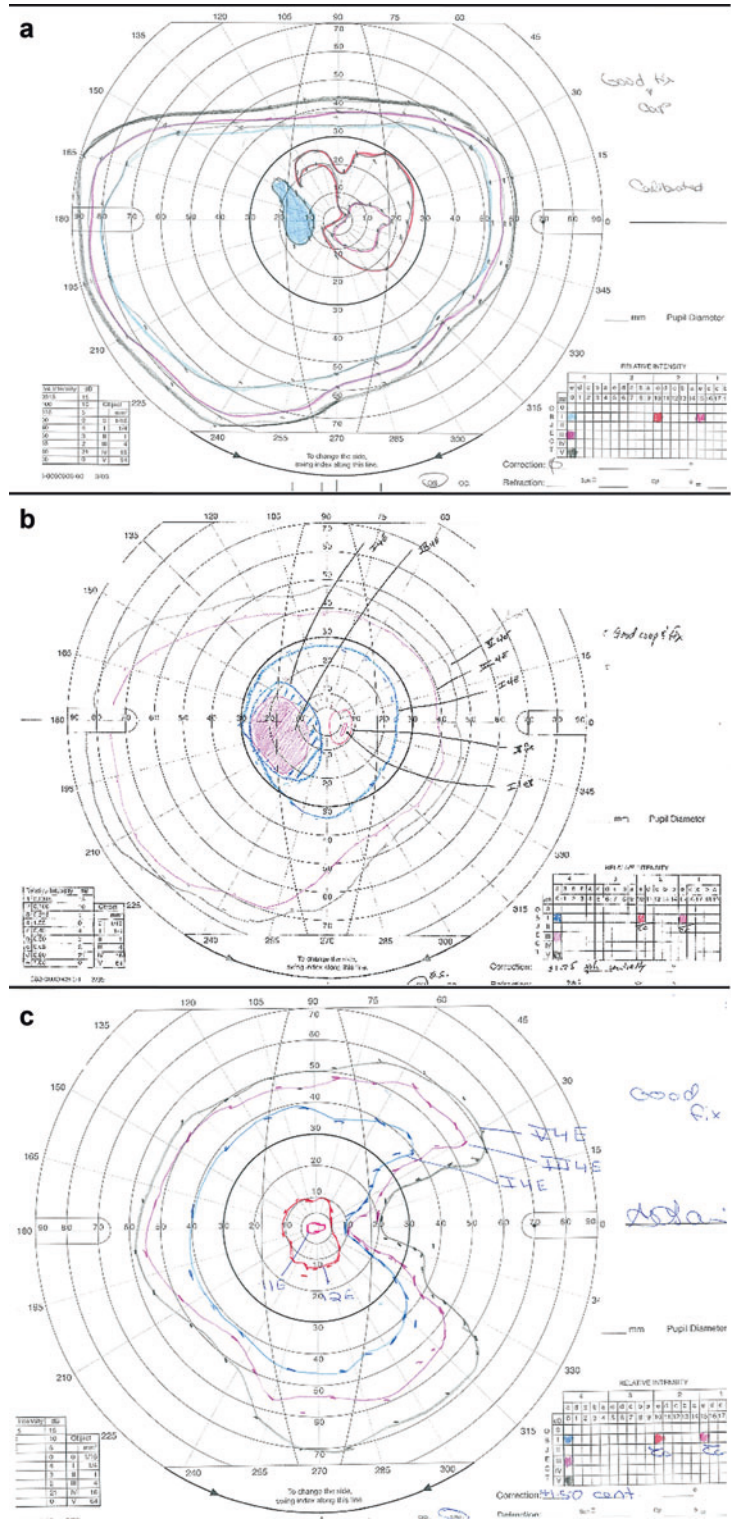
Fundus Autofluorescence

Autofluorescence imaging in AZOOR varies based on the type of presentation and degree of outer retinal disruption. Increased lipofuscin deposition within RPE cells that are metabolizing adjacent photoreceptor break down products results in hyperautofluorescence. With minimal photoreceptor damage, lipofuscin accumulation in underlying RPE cells is limited, and the region can be isofluorescent. On the contrary, in eyes with larger regions of photoreceptor damage, lipofuscin accumulation at the adjacent RPE cells increases, thus increasing FAF in corresponding regions (Fig. 6e, f). This can be seen in both occult and overt cases.

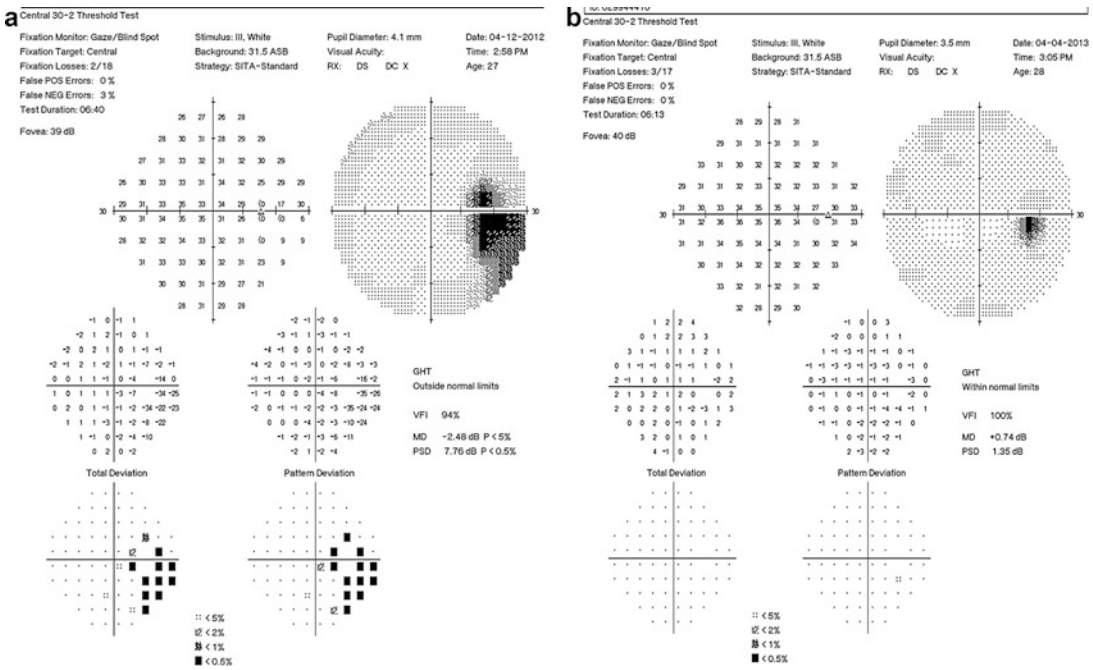
In a subset of AZOOR cases, hyperautofluorescence can be seen at the leading edge or "delineating line" of the lesion (Fig. 7f; Spaide 2004). With time, the FAF pattern within the delineating zone can become speckled and less prominent, which has been described in subacute lesions (Mrejen et al. 2014). Within this zone, increased autofluorescence can be found due to lipofuscin-laden RPE cells. Over time, the region turns hypoautofluorescent as a result of RPE cell apoptosis. As would be expected, these hypoautofluorescent regions correspond to hyperfluorescent zones on FA and ICG as described previously (Fig. 7d).

Optical Coherence Tomography

With recent advances in SD-OCT, imaging has been vital in identifying outer retinal disruption



Acute Zonal Occult Outer Retinopathy (AZOOR), Fig. 3 Goldmann visual fields of three different patients with AZOOR. All three (**a**–**c**) reveal enlarged blind spots and temporal field defects



Acute Zonal Occult Outer Retinopathy (AZOOR), Fig. 4 30-2 Humphrey visual field of a patient with occult unilateral AZOOR at (**a**) initial presentation revealing enlarged blind spot and (**b**) at 1 year revealing resolved visual field defect. This patient also recovered outer retinal SD-OCT features following treatment with systemic corticosteroids and acyclovir, as demonstrated in Fig. 8

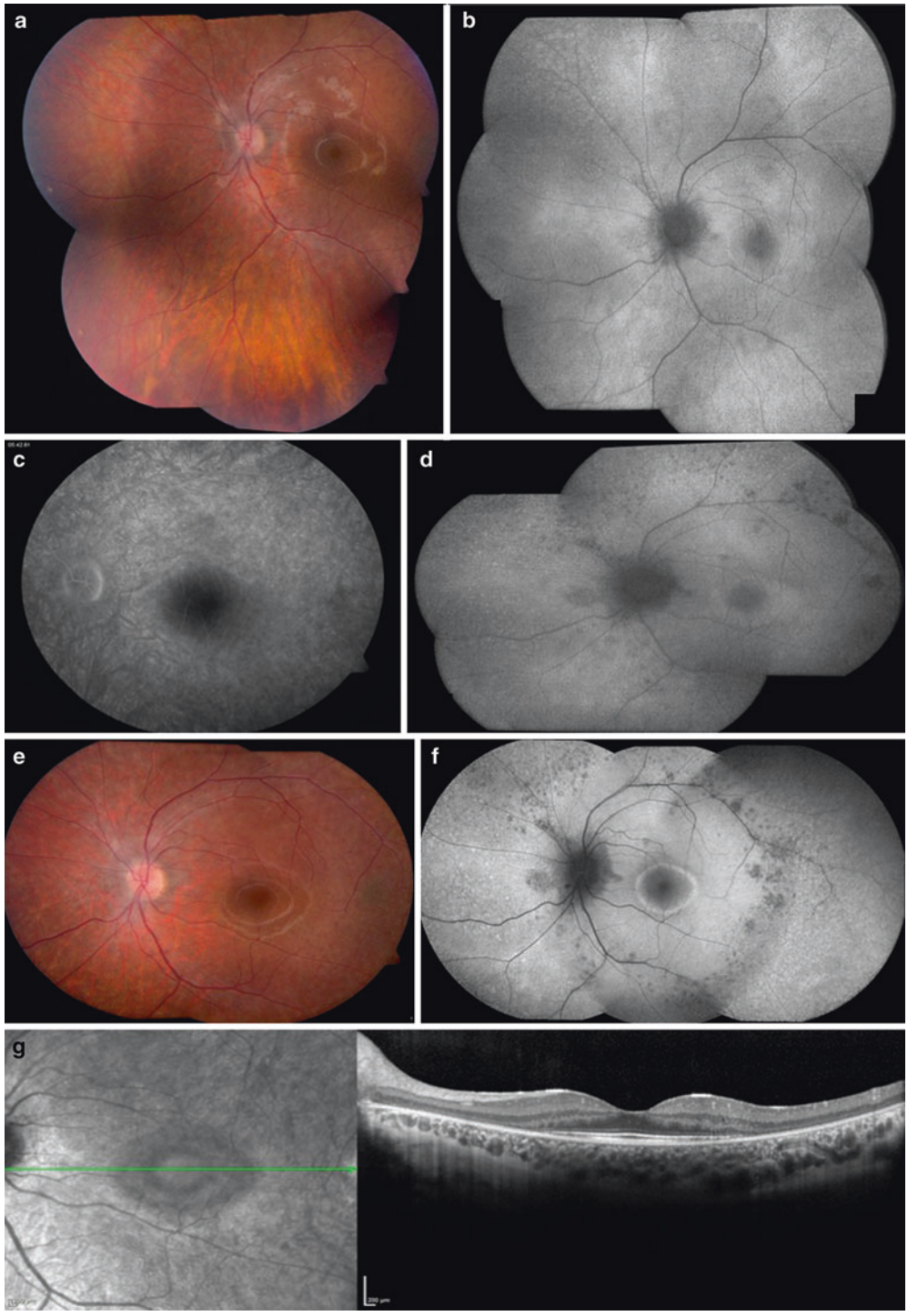
in AZOOR and AZOOR complex diseases. OCT scans corresponding to regions of visual field loss have revealed decreased ellipsoid zone and photoreceptor outer segment reflectivity, representing damage to outer segment cellular processes (Mrejen et al. 2014; Li and Kishi 2007; Spaide et al. 2008; Makino and Tampo 2013). Outer plexiform layer thickening with loss of the outer nuclear layer has also been described. In some patients that are treated early in the disease course, the outer retinal layers on SD-OCT can undergo reconstitution as the cells recover some or all function (Figs. 8 and 9). However, if actual receptor cell loss occurs, recovery of the outer retinal layers and visual field are unlikely (Fig. 10).

Electroretinogram

Electroretinogram (ERG) alterations depend on the degree of photoreceptor disruption. In eyes with unilateral or focal field loss, the ERG can be reduced compared to the normal fellow eye (Figs. 11 and 12). A subnormal ERG response can occur in eyes with extensive photoreceptor damage and visual field loss. The ERG alteration can be scotopic, photopic, or both depending on the region of photoreceptors affected by AZOOR. In bilateral cases, subnormal ERGs can be present in both eyes depending on the degree of outer retinal involvement. Asymmetric ERG responses between eyes, as described by Gass et al. and Jacobson et al., can be present, if the eyes have asymmetric manifestations of the disease (Gass et al. 2002; Jacobson 1996). Multifocal ERG tests cone function within the macula and can be valuable in identifying the location of visual field loss and degree of photoreceptor disruption. However, it may not be able to detect occult rod disruption outside the macula.

Pathogenesis

The exact etiology of AZOOR is unknown. However, Gass proposed a viral or other infectious



Acute Zonal Occult Outer Retinopathy (AZOOR), Fig. 5 (continued)

etiology for the syndrome (Gass 1993; Gass et al. 2002). Gass postulated that a virus or other infectious agent invades either at the ora serrata or the optic disc margin and propagates into the photoreceptor cells. These anatomical sites are the only two sites where the photoreceptors are not isolated from the systemic circulation by surrounding neuroepithelium. He hypothesized that, after invading the photoreceptors, cell to cell spread of this agent occurs without initially compromising photoreceptor function during an asymptomatic "preclinical phase." Later, in the "acute symptomatic phase," infected cell dysfunction is triggered by the host's immune response. Either a change in the antigenicity of the infective agent or a local autoimmune reaction to the receptors laden with this infective agent triggers photoreceptor dysfunction.

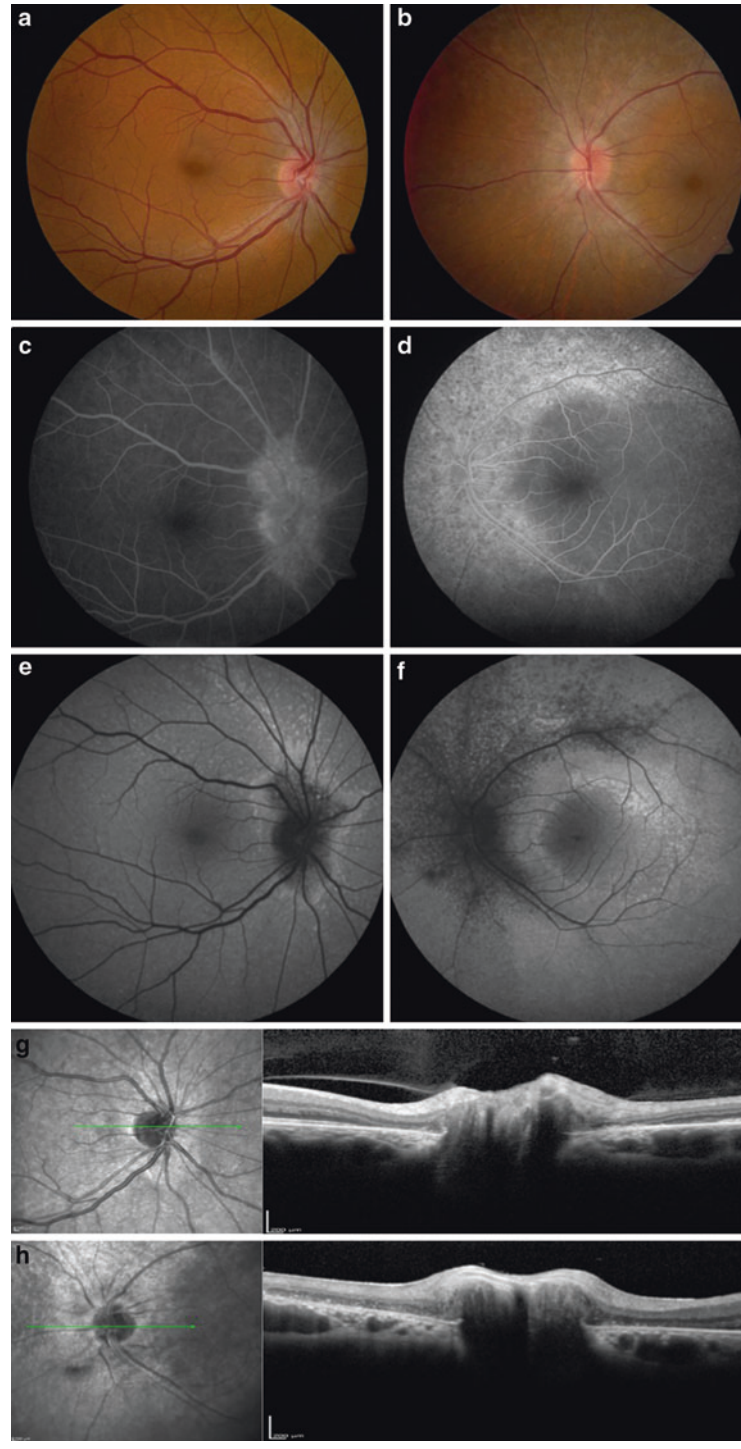
In a subset of AZOOR patients, this immune response results in impaired cell function that causes visual symptoms such as photopsias and visual field loss, but does not induce cell death. Long-term clinical or pathologic evidence of inflammation of the affected photoreceptor cell is absent in them. In others, the receptor cell bodies are destroyed, resulting in secondary RPE changes, bone spicule formation, and permanent visual field defects. Despite recovery of photoreceptors in some cases, retinal cell dysfunction likely persists in most eyes, thus explaining why photopsias can be chronic and visual field defects remain. Stabilization of visual fields and recovery of function typically occurs 6 months after the onset of symptoms; however, longer times to stabilization have been reported. Moreover, despite stabilization of the symptoms and visual field loss, disease recurrence and increased visual field loss can occur many months to years after the onset of symptoms in some.

In the other subset of patients, the immune response is strong enough to induce photoreceptor cell death. In these, vitreous inflammation, perivascular exudation, and optic disc edema can develop, likely as an epiphenomenon to the retinal receptor cell death. This inflammatory response becomes clinically evident in the weeks following the onset of symptoms and seems to vary depending on the degree of retinal involvement (Gass et al. 2002). Over time, in both occult and overt cases, retinal vascular narrowing, perivascular sheathing, and reactive changes to the RPE can develop. Impaired interaction of the microvilli between the photoreceptors and RPE causes migration of the RPE towards the inner retina resulting in a bone spicule appearance.

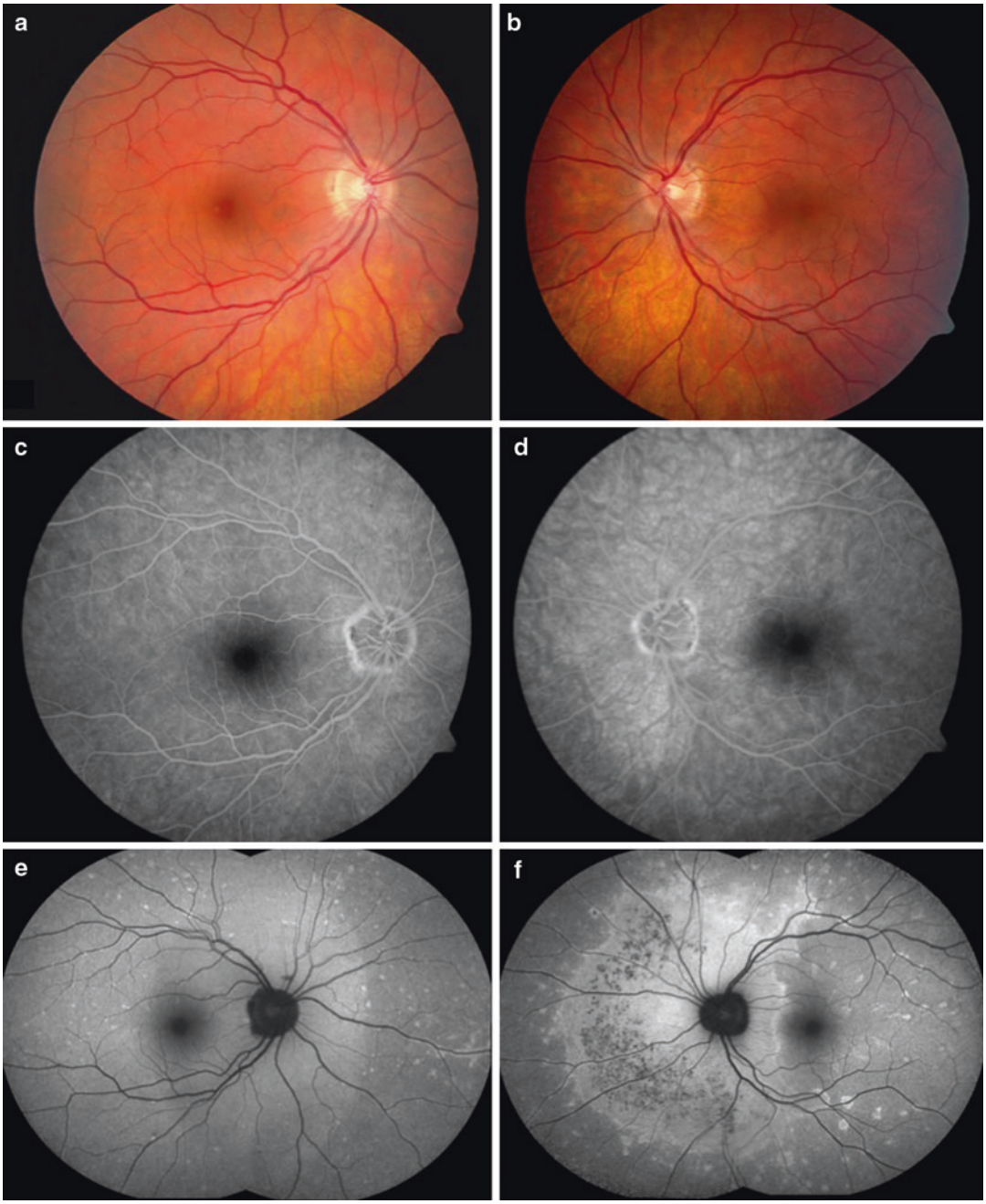
Autoimmunity

An autoimmune mechanism in the pathogenesis of AZOOR has been suggested, but the evidence is limited (Weleber et al. 2005; Heckenlively and Ferreyra 2008; Ara-Iwata et al. 1996). Anti-recoverin, anti-enolase, and other less common anti-retinal antibodies have been identified in individuals with cancer-associated retinopathy (CAR) and melanoma-associated retinopathy (MAR). In addition, these antibodies have been identified in cancer-free patients who have complained of photopsia, nyctalopia, and visual field loss. In a

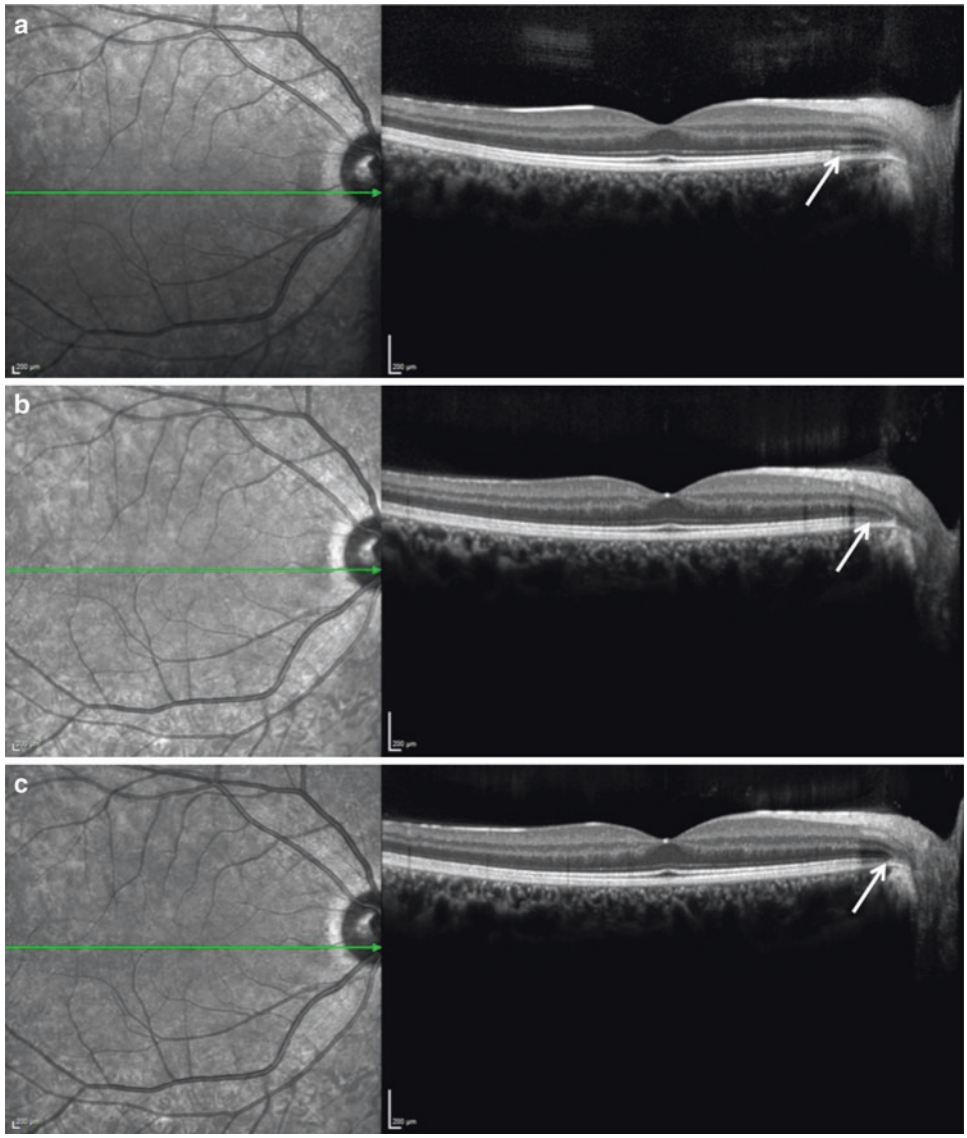
Acute Zonal Occult Outer Retinopathy (AZOOR), Fig. 5 Imaging of left eye of a patient with bilateral overt AZOOR. (**a**) Montage color photograph revealing subtle peripapillary pigment changes corresponding to hypoautofluorescence (hypo AF) on FAF imaging (**b**). (**c**) Fluorescein angiography in arteriovenous phase without any significant leakage or staining and (**d**) follow-up FAF demonstrating peripapillary hypo AF and scattered regions of hypo AF nasally, temporally, and along the vascular arcades. (**e**) Color photograph demonstrating increased pigment atrophy in the peripapillary, nasal, and nasal macula regions. (**f**) FAF imaging on subsequent follow-up revealing peripapillary hypo AF, patchy areas of hyperautofluorescence (hyper AF) interspersed with areas of hypo AF, and ring of hyper AF perifoveally. (**g**) SD-OCT imaging revealing loss of ellipsoid zone nasal and temporal to the fovea with thinning of the outer nuclear layer. Follow-up OCTs are presented in Fig. 10



Acute Zonal Occult Outer Retinopathy (AZOOR), Fig. 6 Patient with bilateral asymmetric AZOOR with peripapillary occult disease (OD) and overt disease (OS). Fundus photography of (**a**) OD revealing normal findings and (**b**) OS revealing peripapillary atrophy extending along the vascular arcades. Fluorescein angiography of (**c**) OD reveals peripapillary staining and (**d**) a wider area of staining from a window defect as a result of outer retinal atrophy in the left eye. (**e**) FAF imaging of right eye revealing a peripapillary border of hyper AF with a region of hypo AF within it and (**f**) left eye revealing marked hypo AF in peripapillary region extending beyond the arcades, which correspond to staining regions on FA. SD-OCT of (**g**) right eye reveals loss of ellipsoid zone in nasal and temporal peripapillary regions and (**h**) left eye delineating marked loss of ellipsoid zone nasally and temporally to the optic nerve

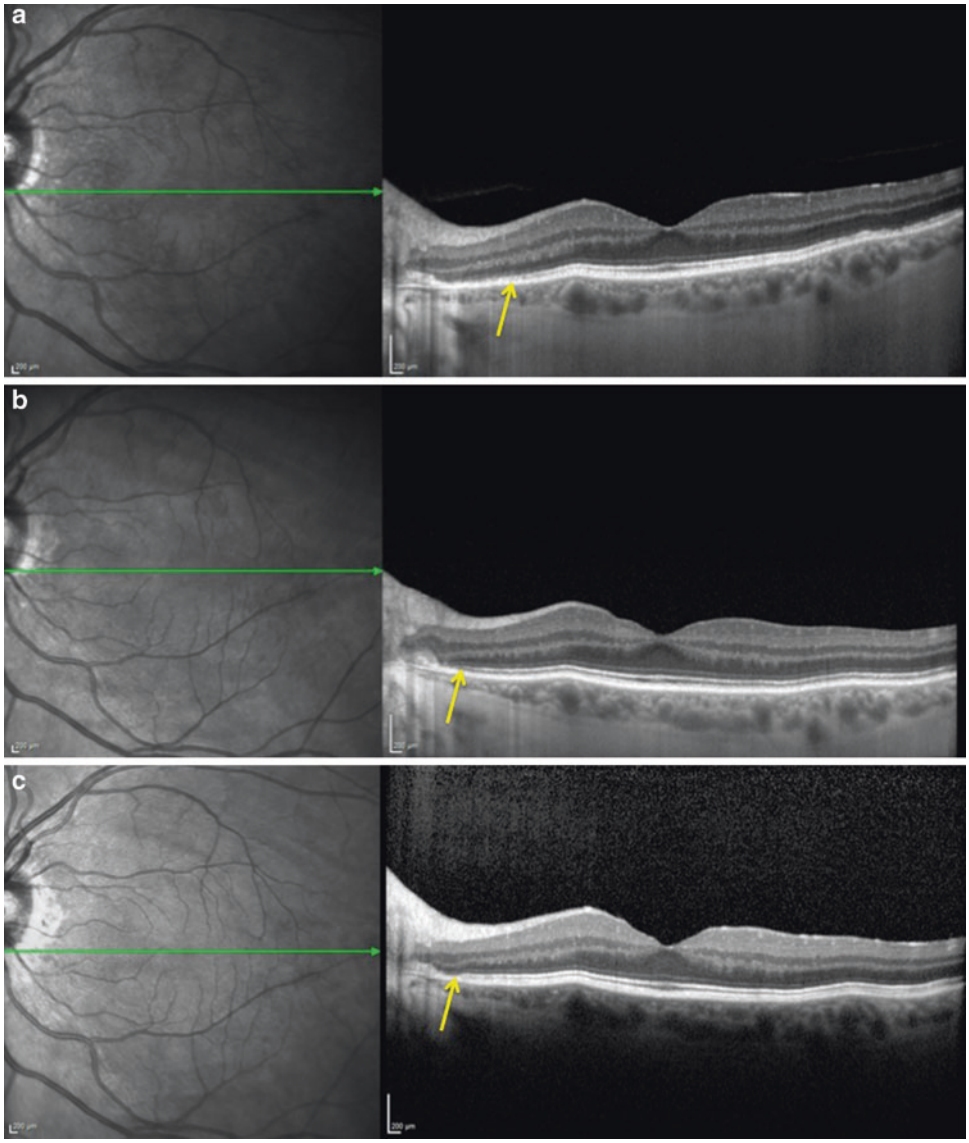


Acute Zonal Occult Outer Retinopathy (AZOOR), Fig. 7 Imaging of patient with bilateral AZOOR who presented with enlarged blind spot and photopsias. Color fundus images of (**a**) right eye revealing normal findings and (**b**) left eye revealing mild peripapillary atrophy. Fluorescein angiography of (**c**) right eye reveals normal study without leakage and (**d**) left eye with mild staining in the peripapillary region. FAF imaging of (**e**) right eye reveals scattered foci of hyper AF and (**f**) left eye with large peripapillary zone of hyper AF with interspersed foci of hypo AF spots. Scattered hyper AF regions are present throughout, the significance of which is not clearly known



Acute Zonal Occult Outer Retinopathy (AZOOR), Fig. 8 SD-OCT images of patient with unilateral occult AZOOR who presented with constant "flickering lights" out of right eye. (**a**) Initial OCT with *white arrow* highlighting border where ellipsoid zone and outer segments are affected. On (**b**) 6 month follow-up, the SD-OCT reveals some recovery of ellipsoid zone as highlighted by *white arrow*. At (**c**) 1 year follow-up, SD-OCT reveals essentially recovered ellipsoid zone. Visual field improvement is highlighted in Fig. 4. There is a subtle change in the temporal juxtapapillary region highlighted in the infrared image corresponding to the OCT changes in (**a**) that normalized in (**c**)

subset of the reported cases, the clinical presentations and symptoms of patients were indistinguishable from those in AZOOR patients. Whether the circulating anti-retinal antibodies found in some patients are causative or an epiphenomenon is debatable. In fact, in a long-term follow-up study, there was a stronger association of autoimmune disease (28%) in AZOOR patients or their first-degree relative (Gass et al. 2002).

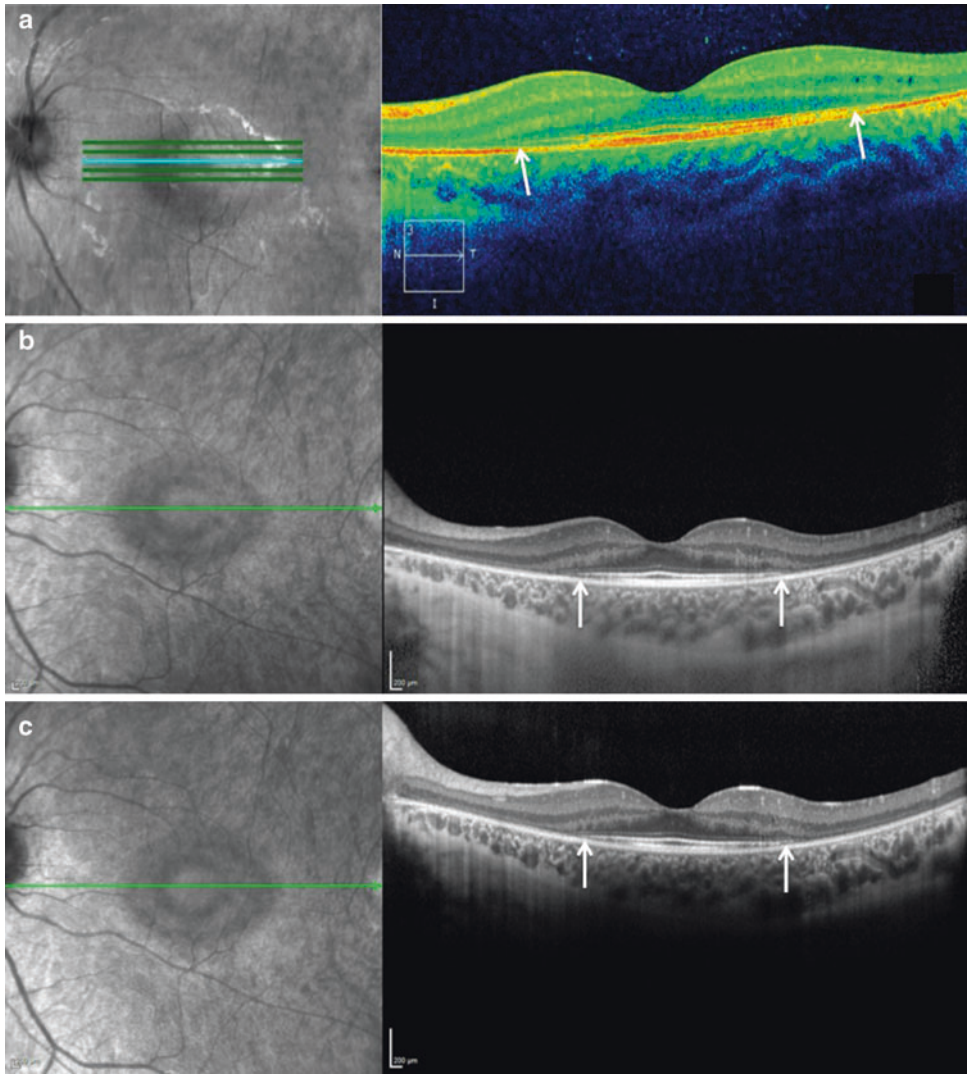


Acute Zonal Occult Outer Retinopathy (AZOOR), Fig. 9 SD-OCT images of a patient with unilateral occult AZOOR from (**a**) initial presentation through most recent follow-up over 2 years (**b**, **c**) revealing progressive improvement in ellipsoid zone as highlighted by *yellow arrow*

Despite this, presently, evidence against an autoimmune mechanism for AZOOR includes lack of consistent identification of anti-retinal antibodies in affected patients and inconsistent effectiveness of immunosuppression or corticosteroids in achieving disease stabilization (Gass 2003). However, a local inflammatory response without circulating systemic anti-retinal antibodies could still have a role in the pathogenesis of AZOOR.

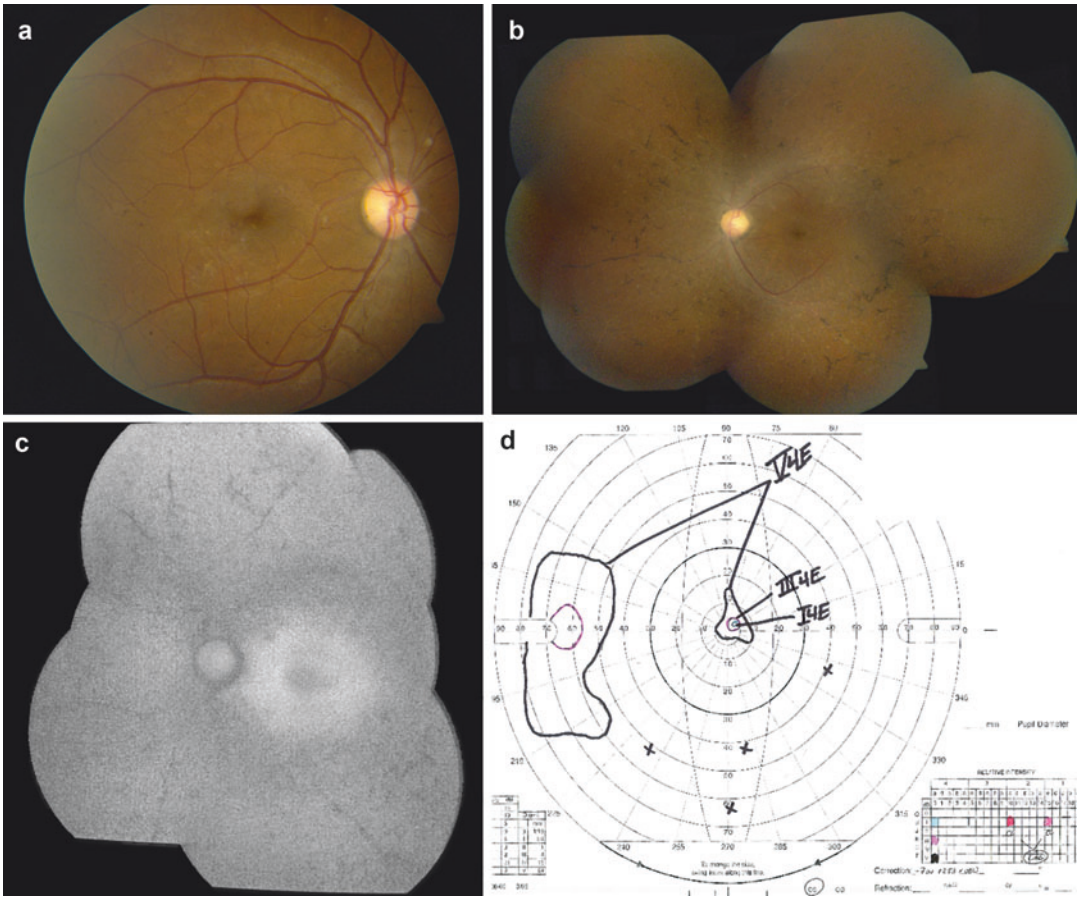
Follow-Up and Clinical Course

The variable presentation of AZOOR creates a variable clinical course based on the initial presentation and subsequent changes. Affected eyes can present with either occult or overt disease, and due to its variable course, a subset of eyes with initial occult disease can develop clinical findings on exam if photoreceptor loss and RPE cell



Acute Zonal Occult Outer Retinopathy (AZOOR), Fig. 10 SD-OCT images of patient highlighted in Fig. 5. (**a**) Initial Zeiss SD-OCT revealing loss of ellipsoid zone with outer nuclear layer thinning nasal and temporal to foveal as highlighted by *white arrows*. Subsequent SD-OCT images over 2 years of follow-up (**b**, **c**) did not reveal any outer retinal recovery

migration occurs over time. In a long-term follow-up study of 51 patients, fundus examination was normal in 90% of patients at presentation and remained normal at follow-up in 52% of eyes (Gass et al. 2002). Visual acuity was 20/40 or better in 75% of patients and remained so in 68% on follow-up. Furthermore, two thirds of patients presented with unilateral involvement, and 75% had bilateral AZOOR at most recent follow-up. In this subset of patients, 72% demonstrated visual field stabilization within 6 months, and 24% showed mild improvement. It can be assumed that those eyes that recovered function did not undergo significant photoreceptor or outer nuclear layer loss. Interestingly, those eyes that presented with significant field loss and visual compromise did not regain function likely because of significant outer retinal cell death within close proximity to central fixation, thus limiting the potential for recovery.



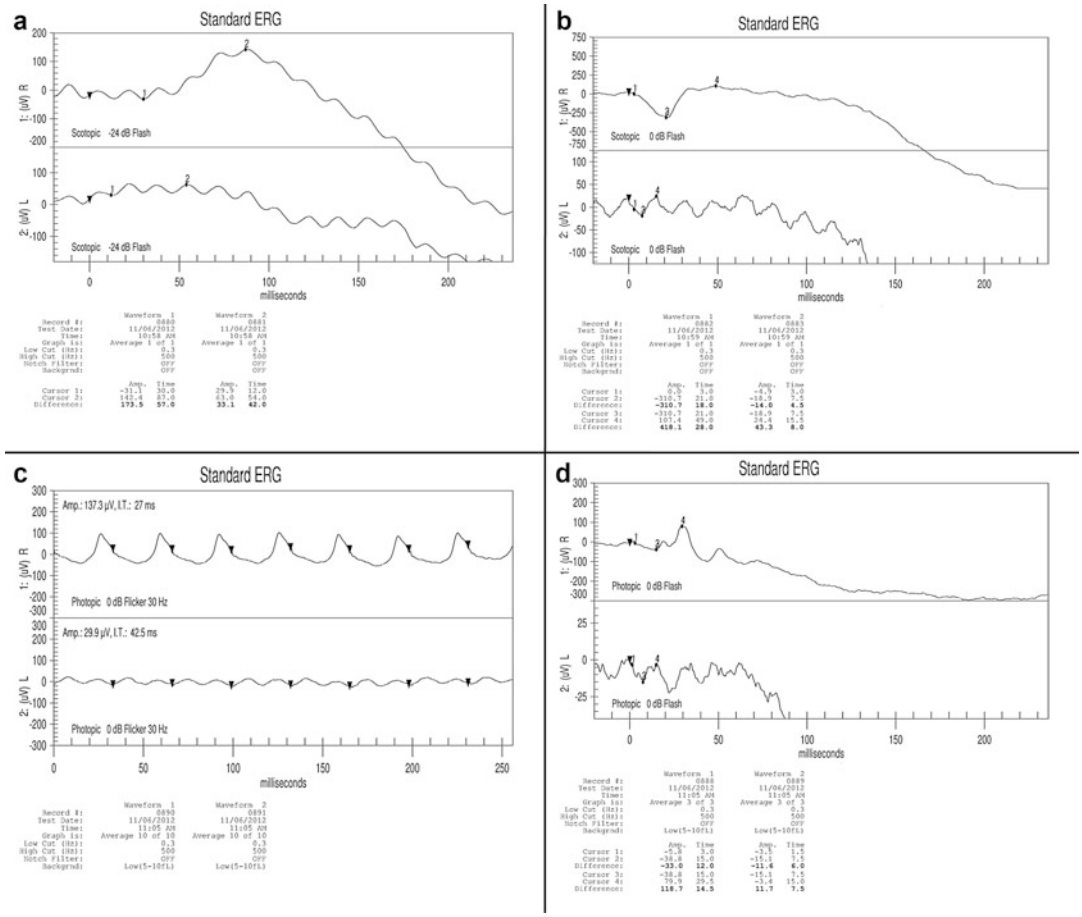
Acute Zonal Occult Outer Retinopathy (AZOOR), Fig. 11 Patient with unilateral advanced AZOOR of the left eye who presented with loss of peripheral vision and transient photopsias for over 1.5 years. Normal exam of (**a**) right eye. Imaging of left eye including (**b**) fundus photograph and (**c**) FAF image revealing diffuse pigment changes and hypo AF with (**d**) severely depressed visual field on GVF exam

Treatment

There has been no definitive treatment that has been able to control the symptoms of AZOOR or induce stabilization or recovery of the visual field loss. However, given the presumed viral etiology and local inflammatory response, use of oral antiviral agents in conjunction with a tapering dose of oral corticosteroids for approximately 6 weeks has been utilized in those patients that present early in the disease course (Gass et al. 2002). Of those treated, a small subset achieved visual field and photoreceptor recovery and even improvement in photopsias. When symptoms persist and field loss progresses despite antiviral or corticosteroid treatment or when symptoms recur following corticosteroid tapering, use of periocular steroid treatment and immunosuppressive agents such as methotrexate, mycofenolate mofetil, and adalimumab can be implemented; however, the response is variable with some patients demonstrating stabilization of field loss and resolution of photopsias (Spaide et al. 2008; Neri et al. 2014).

AZOOR Complex Disorders

A small percentage of patients diagnosed with MFC, PIC, MEWDS, and AMN can present with photopsias and visual field loss similar to



Acute Zonal Occult Outer Retinopathy (AZOOR), Fig. 12 ERG of patient in Fig. 11 demonstrating depressed rod and cone responses of left eye compared to right eye on (**a**) scotopic −24 dB impulse (rods), (**b**) scotopic – 0 dB impulse (rods and cones), (**c**) 30 Hz flicker (cones), and (**d**) photopic impulse (cones)

symptoms of AZOOR (Gass 2003; Jampol and Wiredu 1995; Zweifel et al. 2009; Holz et al. 1994). Gass proposed that these disorders were part of a spectrum of a single disorder known as the "AZOOR complex"; however, controversy remains whether these disorders are necessarily related. Unless a definitive overt manifestation of AZOOR is present, differentiating the AZOOR Complex disorders from AZOOR based on imaging alone can be challenging (Mrejen et al. 2014). Furthermore, these disorders are classified based on clinical presentation rather than etiology. Until discrete etiologies of the individual disorders are understood, grouping them into AZOOR complex disorders may be easier as long as it is understood that they each have unique characteristics in addition to possessing the common features of field loss and photopsias (Zweifel et al. 2009; Holz et al. 1994; Taira et al. 2006).

Acute Annular Outer Retinopathy

In the few documented cases of AAOR, patients present with acute loss of visual field similar to AZOOR, but with a concurrent gray-white ring bordering the zone of field loss. The clinical spectrum (permanent versus variable pigmentary changes), fluorescence patterns on angiography, and response to corticosteroid therapy are variable.

This disease is believed to be a subset of AZOOR that is accompanied by field loss and clinical findings of retinal whitening at the border of the zone of field loss (annular type) or whitening of the entire zone (overt type) (Gass and Stern 1995; Fekrat et al. 2000; Cheung et al. 2002; Harino et al. 2004; Mitamura et al. 2005; Tang et al. 2008).

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Acuvail

▶ Ketorolac Tromethamine

Add-On Intraocular Lens

▶ Piggyback Intraocular Lens

Adenoid Cystic Carcinoma

▶ Cylindroma of Eyelid

Adenoma of the Clear Cell Type

▶ Hidradenoma, Clear Cell (Eccrine Acrospiroma)

Adenoviral Keratoconjunctivitis

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Synonyms

Acute conjunctivitis; Follicular conjunctivitis; Pink eye; Pseudomembranous conjunctivitis; Red eye

Definition

Adenoviral conjunctivitis is an inflammatory condition that affects the bulbar and palpebral conjunctiva as a result of an adenovirus infection.

Etiology

Adenoviruses, which are nonenveloped DNA viruses, are the most common cause of viral conjunctivitis. Of the 41 adenovirus serotypes, 19 can cause conjunctivitis. These infections are highly infectious, spreading via respiratory droplets or direct contact from fingers to the lids and conjunctival surface or in swimming pools. The incubation period is usually 5–12 days, and the clinical illness is present for 5–15 days. The two main infections of adenoviral conjunctivitis are:

Pharyngoconjunctival fever (PCF): Associated with systemic infection and is produced by adenovirus serotypes 3, 4, and 7.

Epidemic keratoconjunctivitis (EKC): The severest ocular disease. Adenovirus serotypes 8, 19, and 37 are the serotypes most commonly associated with EKC (Sambursky et al. 2006; Yanoff et al. 2009).

Clinical Presentation

It usually starts in one eye and spreads to the other several days later. It is frequently associated with exposure to an infected person or recent upper respiratory tract symptoms. Patients complain of a red eye, burning, or a foreign body sensation that is associated with a watery to mucous discharge and preauricular lymphadenopathy. Corneal subepithelial infiltrates may be present late in the course (Krachmer et al. 2011).

Pharyngoconjunctival Fever (PCF)

It is characterized by a combination of pharyngitis, fever, conjunctivitis, and adenopathy. Diarrhea or rhinitis might be present. The conjunctivitis is predominantly follicular with a scant watery discharge, hyperemia, and mild chemosis. PCF usually affects both eyes, with one eye generally affected more severely. In comparison with other types, PCF is more systemic with less corneal involvement (Yanoff et al. 2009; Sambursky et al. 2006).

Epidemic Keratoconjunctivitis (EKC)

The conjunctivitis is more severe than PCF. EKC produces a more follicular response of the conjunctiva with a watery discharge, hyperemia, chemosis, and ipsilateral preauricular lymphadenopathy. Subconjunctival hemorrhages, conjunctival membrane formation, and lid edema are common. Up to 50% of patients have only unilateral infection. One of the distinguishing features of EKC is corneal involvement. Focal epithelial keratitis may develop 1 week after the onset, characterized by central ulceration with gray-white dots, and they may persist for 2 weeks. Two weeks after the onset of symptoms, subepithelial infiltrates (SEI) can appear beneath the focal epithelial lesions (Sambursky et al. 2006; Yanoff et al. 2009).

Diagnosis

The diagnosis is usually made clinically, but confirmation of the disease by culture or polymerase chain reaction (PCR) is needed in certain situations. The clinical diagnosis of viral conjunctivitis can be based on the presence of acute conjunctivitis and one of the following features: follicles on the inferior tarsal conjunctiva, preauricular

lymphadenopathy, an associated upper respiratory infection, and a recent contact with a person with a red eye. If the diagnosis is not readily apparent, laboratory studies may be helpful in determining etiology (Sambursky et al. 2006; Krachmer et al. 2011).

Differential Diagnosis

Differential diagnosis includes other viral conjunctivitis, bacterial conjunctivitis, keratitis, allergic conjunctivitis, and toxic conjunctivitis.

Prophylaxis

It is very crucial to avoid personal contact. The patient is considered infectious until redness and tearing are gone; during this period, patients should minimize the risk of spreading the infection to others by washing their hands and avoiding sharing personal items. Cleaning the instruments that have been used during the examination is very important.

Therapy

Most cases of viral conjunctivitis resolve spontaneously, without sequelae, within days to weeks. Treatment is usually supportive with cold compresses and artificial tears. Pseudomembranes and membranes should be removed when detected. Topical corticosteroid might be used to reduce the inflammation, but these agents should be prescribed with caution. Topical corticosteroid could be used in cases with membranous or pseudomembranous conjunctivitis, iridocyclitis, severe keratitis, and persistent SEIs with visual loss (Yanoff et al. 2009; Krachmer et al. 2011).

Prognosis

Viral conjunctivitis is a self-limited process. The symptoms frequently get worse in the first 3–5 days, with very gradual resolution over the following 1–2 weeks. Some cases might develop corneal scar or symblepharon (Yanoff et al. 2009; Krachmer et al. 2011).

Epidemiology

The annual incidence of acute infectious conjunctivitis in primary care in the developed world has been estimated at 1.5–2%. Conjunctivitis accounts for 30% of all eye complaints in the USA. Of the infectious agents, viral conjunctivitis is most common, accounting for up to 50%.

Cross-References

- ▶ Conjunctivitis
- ▶ Red Eye
- ▶ Subepithelial infiltrate

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Adhesive

▶ Tissue Adhesives, Cyanoacrylate, for Anterior Segment

Adie Syndrome

▶ Anisocoria: Big Pupil

▶ Tonic Pupil (Adie's Pupil), Pharmacological Testing for

Adie's Pupil

▶ Adie's Pupil (Tonic Pupil), Pharmacologic Testing

Adie's Pupil (Tonic Pupil), Pharmacologic Testing

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Synonyms

Adie's pupil; Adie's tonic pupil; Holmes-Adie syndrome

Definition

A tonic pupil is typically dilated in the acute setting and the pupil that reacts slowly or not at all to light but shows a more definite tonic response to accommodation (i.e., light-near dissociation).

Etiology

The tonic pupil is caused by damage to the parasympathetic ciliary ganglion. The parasympathetic innervation to the iris and ciliary body travels with the third cranial nerve and synapses in the ciliary ganglion. This damage is usually due to inflammation from a viral or bacterial infection but can be due to trauma, orbital surgery, or rarely in association with systemic autonomic neuropathies (e.g., Ross syndrome). After the initial insult, reinnervation and upregulation of the postsynaptic receptors occurs, a process known as denervation supersensitivity. The number of axons that travel to the ciliary body is about 30 times the number that supplies the pupil. Due to aberrant reinnervation, fibers formerly supplying the ciliary body travel instead to the pupil.

Clinical Presentation

Patients may be asymptomatic or can present with a dilated and tonic pupil which responds poorly or does not constrict in response to light but reacts to near. There may be loss of deep tendon reflexes in the full Holmes-Adie syndrome.

Diagnostics

Diagnosis is made by clinical exam and topical confirmation with low-dose topical pilocarpine testing. Clinical exam will often show sector paresis of the iris sphincter or vermiform iris movements. Low-dose topical (1/8%) pilocarpine may constrict the tonic pupil due to cholinergic denervation supersensitivity. A normal pupil typically will not constrict with such a dilute dose of pilocarpine.

Differential Diagnosis

Traumatic iris damage, third cranial nerve palsy, pharmacological dilation, and iris rubeosis

Therapy

Prescription of asymmentric reading glasses can be used to correct for the accommodative visual impairment of the eyes. Pilocarpine low-dose

drops may be administered to constrict the affected pupil.

Prognosis

There is no mortality rate relating to the idiopathic tonic pupil (i.e., Adie's tonic pupil) but the systemic autonomic neuropathies (e.g., Ross syndrome) may have other potentially life-threatening parasympathetic problems (e.g., GI, cardiac, temperature regulation).

Epidemiology

Adie's tonic pupil most commonly affects younger women, with a 2.6:1 female preponderance. The mean age of the onset is 32 years. In 80% of cases, it only affects one eye but can become bilateral over time.

Cross-References

- ▶ Adie's Tonic Pupil
- ▶ Anisocoria

Further Reading

Bruyn GW, Gooddy W (2000) Adie's syndrome. In: Koehler PJ, Bruyn GW, Pearce JMS (eds) Neurological eponyms. Oxford University Press, New York, p 181

Adie's Tonic Pupil

- ▶ Adie's Pupil (Tonic Pupil), Pharmacologic Testing
- ▶ Anisocoria: Big Pupil
- ▶ Tonic Pupil (Adie's Pupil), Pharmacological Testing for

Adrenal Cortical Steroid

- ▶ Corticosteroids

Adult-Onset Foveomacular Vitelliform Dystrophy

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Synonyms

Adult-onset vitelliform macular dystrophy (AVMD); Gass disease; Pseudo-Best (disease); Pseudo-vitelliform (macular dystrophy)

Definition

Adult-onset foveomacular vitelliform dystrophy (AOFVD) is a macular dystrophy sharing phenotypic features with Best's disease, with onset in the adult age (between the fourth and sixth decades) (Gass 1974). Sharp distinction between AOFVD and pattern dystrophies may be difficult (Deutman et al. 2006).

Etiology

The mechanism underlying the physiopathology of AOFVD is still unknown, but it has been postulated that there is an abnormal accumulation of lipofuscin that may be caused by the increased workload of metabolism and phagocytosis on the RPE cells in conjunction with other disease-related factors (such as age, genetic predisposition, and environmental causes). As a result, the RPE layer is separated from the photoreceptor layer by hyperreflective material (Arnold et al. 2003). Mutations in the genes *BEST1* (11q12), *PRPH2* (6p21.1), or *IMPG1* (6q14.2-q15) (encoding bestrophin-1, peripherin and SPACR, respectively) have been found in some

individuals with AOFVD (Felbor et al. 1997; Allikmets et al. 1999; Kramer et al. 2000).

Clinical Presentation

The clinical onset is typically in the adult age, between the fourth and sixth decade of life (with a ratio M = F). In the early stages of AOFVD, patients are asymptomatic or have mild complaints of scotoma, visual blur, or metamorphopsia in one or both eyes (Gass 1974). On the other hand, significant visual impairment can result in patients with advanced stages or large atrophic lesions. Choroidal neovascularization (CNV) may develop in early as well as advanced stages.

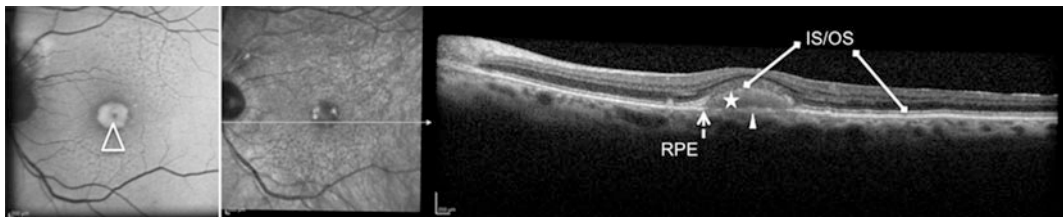
Different progressive stages can be defined on the basis of fundus examination, similarly to Best's disease or vitelliform macular dystrophy (Gass 1997; Querques et al. 2011). The vitelliform stage is characterized by a well-circumscribed, typically 0.5- to 1-disk-diameter, "egg-yolk" lesion (i.e., the yellow material) within the macula (Figs. 1 and 2a). The pseudohypopyon stage is characterized by the yellow material that accumulates inferiorly (Fig. 3) and is followed by partial reabsorption of the material (scrambled-egg lesion) in the vitelliruptive stage (Fig. 4). Development of macular atrophy or fibrosis characterizes the final stages of the disease (Fig. 2b). However, the disease is clinically heterogeneous and pleomorphic, with extreme variability in the size, shape, and distribution of the yellowish material. These stages do not always occur consecutively nor do they occur inevitably in all patients.

Diagnostics

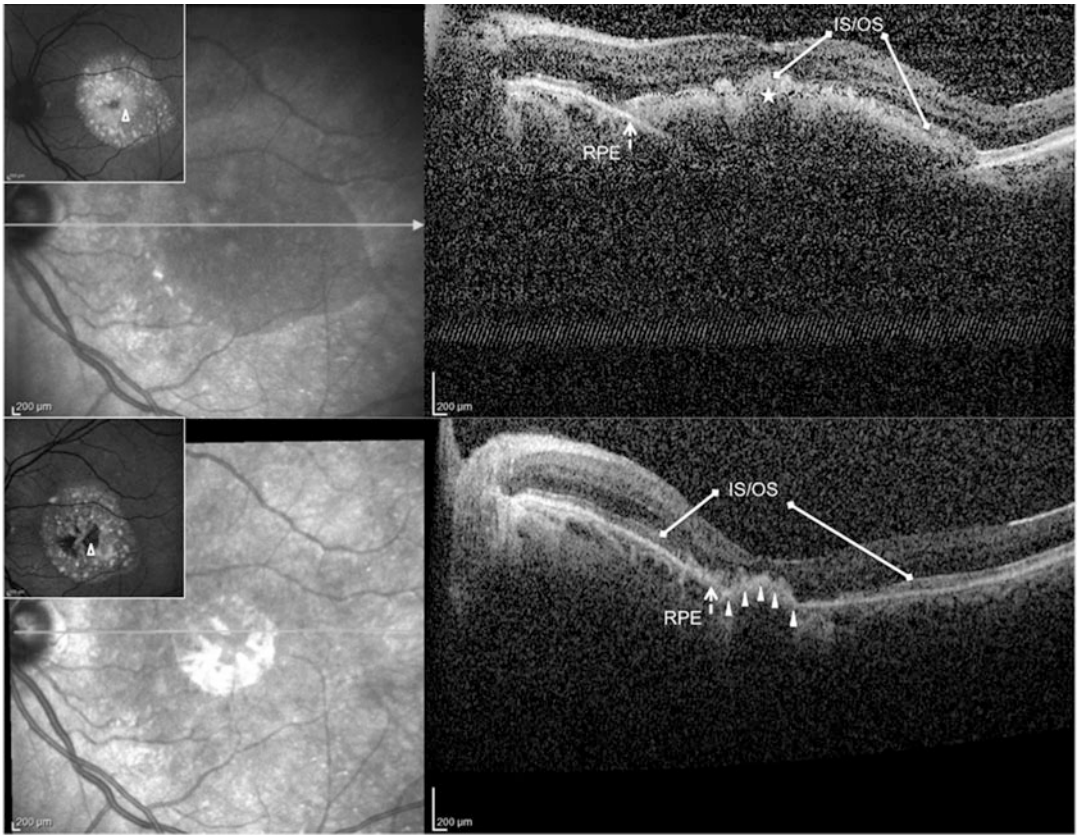
Multimodal imaging is particularly useful to make diagnosis of AOFVD. Fundus autofluorescence (FAF) and spectral-domain optical coherence tomography (SD-OCT) represent the main noninvasive imaging techniques to make the diagnosis and monitoring AOFVD (Querques et al. 2011).

In the vitelliform stage of the disease, FAF shows unilateral/bilateral and symmetric/asymmetric subretinal, oval or round, central intense hyperautofluorescence (Figs. 1 and 2a). In the pseudohypopyon stage, FAF shows loss of autofluorescence, particularly, in the upper part of the lesion in the pseudohypopyon stage (Fig. 3) and centrally with an increased amount of the autofluorescence at the outer border of the lesion in the vitelliruptive stage (Fig. 4). FAF shows central hypoautofluorescence in more advanced stage (Fig. 2b).

On SD-OCT, AOFVD is characterized by dynamic alternating phase of accumulation and reabsorption of hyperreflective material in the subretinal space, ending with atrophy or fibrosis. Alterations of the status of central photoreceptors,



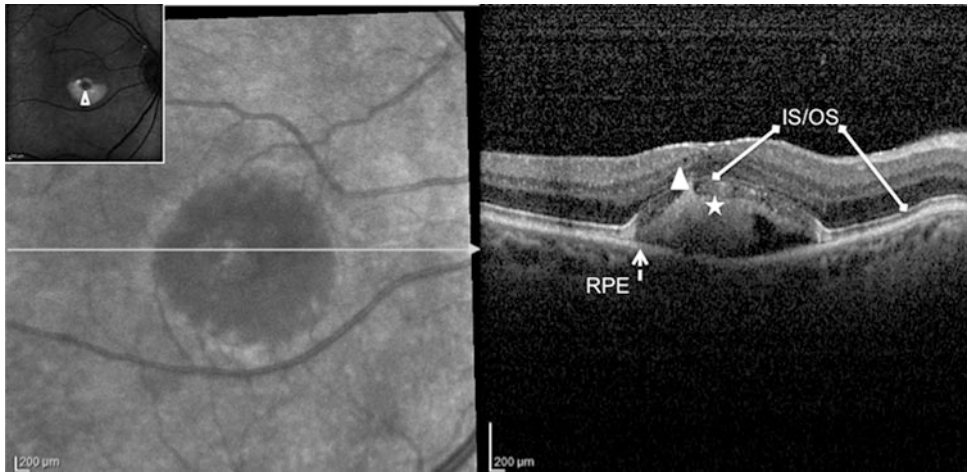
Adult-Onset Foveomacular Vitelliform Dystrophy, Fig. 1 Fundus autofluorescence (*FAF*) and spectral-domain optical coherence tomography (*SD-OCT*) in a patient with adult-onset foveomacular vitelliform dystrophy, presenting the vitelliform stage. FAF shows central hyperautofluorescence (*right panel*) (*open arrowhead*). SD-OCT showed the lesion as hyperreflective (*asterisk*), as well as hyperreflective drusen-like focal nodules (*solid arrowhead*) at the level of retinal pigment epithelium (*RPE*)/Bruch's membrane (*dotted arrows*) within the lesion area. Central interface of the inner and outer segments (*IS/OS*) of the photoreceptors appear "disrupted" (*left panel*) (Reprinted from Querques et al. (2011), with permission from Elsevier)



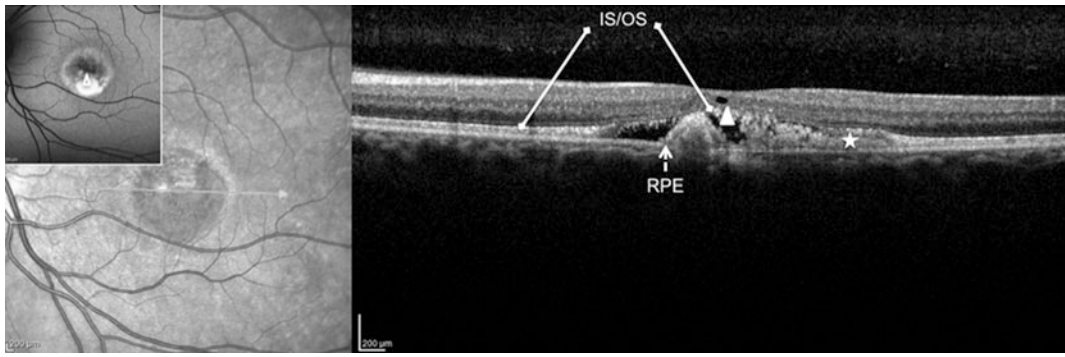
Adult-Onset Foveomacular Vitelliform Dystrophy, Fig. 2 Fundus autofluorescence (*FAF*) and spectral-domain optical coherence tomography (*SD-OCT*) in a patient with adult-onset foveomacular vitelliform dystrophy, presenting the vitelliform stage at baseline (**a**) and the atrophic stage 24 months later (last visit) (**b**). FAF showed central hyperautofluorescence at baseline (*top left*, *small panel*) (**a**) and central hypoautofluorescence at last visit (*bottom left*, *small panel*) (*open arrowhead*) (**b**). SD-OCT showed the lesion as hyperreflective at baseline (*top right panel*) (*asterisk*) (**a**). An atrophic lesion appeared at last visit (*bottom right panel*) (**b**); also, elevation of retinal pigment epithelium (*RPE*, *dotted arrow*) with hyperreflectivity inside (*solid arrowheads*) appeared within the lesion area. Central interface of the inner and outer segments (IS/OS) of the photoreceptors appeared "disrupted" at baseline (*top left panel*) (**a**) and "absent" at last visit (*bottom left panel*) (**b**). SD-OCT showed an overall decrease of lesion size (Reprinted from Querques et al. (2011), with permission from Elsevier)

degree of lesion reflectivity, presence of hyperreflective nodules at the level of RPE/Bruch's membrane, and elevation of RPE can be detected on SD-OCT (Table 1).

In the vitelliform stage, SD-OCT shows hyperreflective subretinal material, as well as hyperreflective drusen-like focal nodules at the level of RPE/Bruch's membrane within the lesion area. In this stage, the central interface of the inner and outer segments (IS/OS) of the photoreceptors may appear disrupted (Figs. 1 and 2a). In the pseudohypopyon stage, SD-OCT shows the lesion as hyperreflective in the inferior part and hyporeflective in the superior part. Central interface of IS/OS of the photoreceptors usually appears disrupted (Fig. 3). In the vitelliruptive stage, SD-OCT shows the lesion as mixed hyperreflective/hyporeflective; elevation of the RPE with hyperreflectivity inside the lesion area may be detected. Central interface of the IS/OS of the photoreceptors usually appears disrupted (Fig. 4). In the advanced



Adult-Onset Foveomacular Vitelliform Dystrophy, Fig. 3 Fundus autofluorescence (*FAF*) and spectral-domain optical coherence tomography (*SD-OCT*) in a patient with adult-onset foveomacular vitelliform dystrophy, presenting the pseudohypopyon stage. FAF shows central hyperautofluorescence (*small panel*) (*open arrowhead*). FAF also clearly shows the sedimentation of the hyperautofluorescence material. SD-OCT shows the lesion as mixed hyperreflective/hyporeflective (*right panel*) (*asterisk*). No hyperreflective drusen-like focal nodules at the level of retinal pigment epithelium (*RPE*)/Bruch membrane or RPE elevations (*dotted arrows*) were evident within the lesion area. Central interface of the inner and outer segments (*IS/OS*) of the photoreceptors appear "disrupted" (*right panel*) (Reprinted from Querques et al. (2011), with permission from Elsevier)



Adult-Onset Foveomacular Vitelliform Dystrophy, Fig. 4 Fundus autofluorescence (*FAF*) and spectral-domain optical coherence tomography (*SD-OCT*) in a patient with adult-onset foveomacular vitelliform dystrophy, presenting the vitelliruptive stage. FAF shows central hypoautofluorescence (*open arrowhead*) concentrically by hyperautofluorescence (*top left*, *small panel*). SD-OCT shows the lesion as mixed hyperreflective/hyporeflective (*right panel*) (*asterisk*); elevation of retinal pigment epithelium (*RPE*) with hyperreflectivity inside appeared within the lesion area (*dotted arrow*). Central interface of the inner and outer segments (*IS/OS*) of the photoreceptors appears "disrupted" (*left panel*). SD-OCT also reveals presence of retinal pseudocysts (*solid arrowhead*) (Reprinted from Querques et al. (2011), with permission from Elsevier)

uncomplicated stage, the central interface of IS/OS of the photoreceptors and the outer retinal layers are usually absent (Fig. 2b).

En face OCT imaging can help visualize the distribution of the vitelliform material in AOFVD (Fig. 5) (Puche et al. 2014).

Adult-Onset Foveomacular Vitelliform Dystrophy, Table 1 Spectral-domain optical coherence tomography features of patients with Adult-Onset Foveomacular Vitelliform Dystrophy (AOFVD)

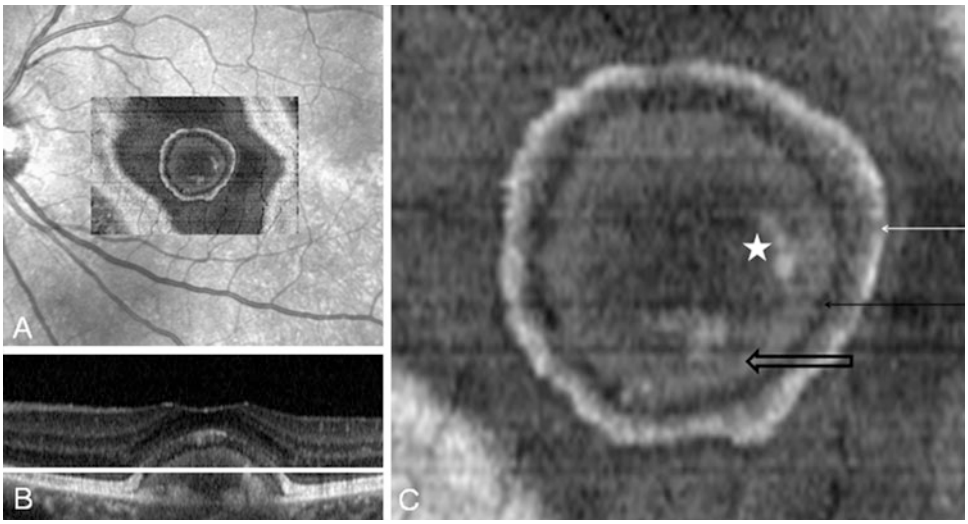
IS/OS interface
Almost normal
Disrupted
Absent
Lesion reflectivity
Hyperreflective
Mixed hyperreflective + hyporeflective
Hyporeflective
Atrophic
Others features
Hyperreflective nodules at the level of RPE/Bruch membrane
Elevations of RPE
Retinal pseudocysts
Subretinal fluid

IS/OS: inner segment/outer segment; RPE:retinal pigment epithelium

Fluorescein angiography (FA) and indocyanine green angiography (ICGA) show a "blocking effect" in the vitelliform and the pseudohypopyon stages due to the accumulation of subretinal material. In the advanced stages of the disease, FA shows hyperfluorescence, which in the early phase is due to RPE defects and chorioretinal atrophy and in the late phase is due to material staining. FA and ICGA are particularly useful if there are signs of presumed CNV.

Differently from Best's disease, electrofunctional tests (both electrooculogram and electroretinogram) are typically normal.

Routine eye examinations, including ancillary exams, are recommended in patients with AOFVD, once or twice a year, to identify any possible complications. CNV is the most frequent complication of AOFVD, occurring with an estimated rate of 11.7% after a 6-year follow-up, and may develop in all stages of the disease. Sudden



Adult-Onset Foveomacular Vitelliform Dystrophy, Fig. 5 Photoreceptors' inner and outer segment (*IS/OS*) interface and interface of the material and photoreceptor in adult-onset foveomacular vitelliform dystrophy visualized by en face optical coherence tomography (*OCT*). Combined infrared reflectance and en face enhanced depth imaging (*EDI*) OCT images (**a**). Horizontal EDI-OCT B-scan (**b**) showed presence of hyperreflective vitelliform lesions between the IS/OS interface and the retinal pigment epithelium (*RPE*). The *dotted line* represents the section plane of the en face EDI-OCT. *En face* EDI-OCT imaging (*magnification*, **c**) showing from the periphery to the lesion centre: IS/OS of the photoreceptor layer, appearing as a hyperreflective ring (*white arrow*); interface of the material and photoreceptor appearing as a hyporeflective ring (*black arrow*); the vitelliform material (*black open arrow*) appearing as round hyperreflective lesion. At the centre of the vitelliform lesion, EDI-OCT shows clusters of intensely hyperreflective RPE elevations or bumps (*white star*) (With kind permission from Springer Graefe's Archive for Clinical and Experimental Ophthalmology, En face enhanced depth imaging optical coherence tomography features in adult onset foveomacular vitelliform dystrophy, 252, 2013, 555-62, Puche et al. (2014), Fig. 1)

drop in visual acuity, presence of hemorrhages or exudates on fundus examination, dye leakage on late FA phases, and hyperfluorescence of the lesion on early and late phases of ICGA are signs of CNV activity; OCT may show increase in foveal thickness.

Differential Diagnosis

Differential diagnosis of AOFVD includes Best's disease, which has typical childhood onset, and, depending on the different stages of the disease, CNV secondary to AMD. Central serous retinopathy and avascular pigment epithelial detachment should also be differentiated from AOFVD.

Therapy

At present, there is no effective therapy for AOVFD. In the absence of any CNV associated with AOFVD, there is no evidence to treat subretinal fluid with anti-VEGF intravitreal drug. Subretinal fluid seems due to debris (unphagocytosed photoreceptor OS) and lipofuscin accumulation in the subretinal space rather than exudative. Treatment of CNV associated with AOFVD by anti-VEGF drugs seems to reduce foveal thickness, but no visual improvement was reported (Mimoum et al. 2013).

Prognosis

The visual prognosis of AOFVD is relatively good in the majority of patients with AOFVD because the disease typically causes uncomplicated slow progressive vision loss. Nonetheless, severe visual lost may be observed.

Epidemiology

AOFVD is an uncommon disease; the exact prevalence is unknown.

Cross-References

- ▶ Age-Related Macular Degeneration
- ▶ Best Vitelliform Macular Dystrophy
- ▶ Central Serous Chorioretinopathy/Choroidopathy
- ▶ Retinal Pigment Epithelium
- ▶ Subretinal Fluid

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Adult-Onset Vitelliform Macular Dystrophy (AVMD)

► Adult-Onset Foveomacular Vitelliform Dystrophy

Afferent Pupillary Defects, Relative (Marcus Gunn Pupil)

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Synonyms

Marcus Gunn pupil

Definition

The relative afferent pupillary defect (RAPD) is a clinical sign. The RAPD is caused by asymmetrical input to the Edinger-Westphal nuclei from the afferent limb of the visual pathway (e.g., retina, optic nerve, chiasm, optic tract, and pretectal neurons). Bilateral and symmetrical afferent system disorders (i.e., symmetric disease in both optic nerves) may not cause a detectable RAPD.

Etiology

Any lesion of the afferent visual pathway from the retina to the optic chiasm, optic tract, and pretectal neurons in the midbrain can result in an RAPD.

Diagnostics

The RAPD is diagnosed via the swinging flashlight test. In this test, a light is alternately shone into the left and right eyes. A normal response displays equal constriction of both pupils, regardless of which eye the light is shone in. A normal response indicates an intact direct and consensual pupillary light reflex. Observing pupil dilatation when the light is swung from the unaffected eye to the affected eye indicates an abnormal response and suggests a defect in the afferent limb of the pupillary light response pathway.

Therapy

Treatment should be directed toward the underlying cause for the RAPD.

Cross-References

► Marcus Gunn Pupil
► RAPD (Relative Afferent Pupillary Defect)
► Swinging-Light Test, for RAPD Identification

Further Reading

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Afferent Visual Pathways

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Definition

Visual information is received by the eye and the signal is relayed by the retina, optic nerve, chiasm, optic tracts, lateral geniculate nucleus, and optic radiations to the striate cortex and extrastriate association cortices for final visual processing.

The eye is the primary sensory organ for vision. It is responsible for collecting and focusing light from the visual environment. Light first passes through the ocular media, consisting of the tear film, cornea, anterior chamber, lens, and the posterior-chamber vitreous. The tear-air interface and cornea have the power to focus light in a fixed manner. The ciliary muscles adjust the shape of the lens in order to dynamically focus light from varying distances upon the retina. Ultimately, the visual image is projected upside down and backward onto the retina.

In the retina, photoreceptors convert photons of light to an electrochemical signal that is relayed to retinal ganglion cells. To arrive at the photoreceptors, light must first pass through transparent inner layers of the neurosensory retina, comprised of the nerve fiber layer, ganglion cells, amacrine cells, and bipolar cells. The photoreceptors contain photopigment consisting of a membrane protein known as opsin and a chromophore molecule called 11-*cis*-retinal. As light reaches the photopigment, it causes a conformational change of 11-*cis*-retinal to all-*trans*-retinal. All-*trans*-retinal has a low binding affinity, so it detaches from the opsin molecule. The free opsin molecule then activates another membrane complex (the G-protein transducin), by replacing a guanosine diphosphate (GDP) molecule with a guanosine triphosphate (GTP) molecule. Activated G-protein transducin stimulates the enzyme phosphodiesterase (PDE), which hydrolyzes the cytoplasmic second messenger cyclic guanosine monophosphate (cGMP). Reduced levels of cGMP cause closure of membrane sodium channels, reducing the inward sodium current and hyperpolarizing the cell. Thus, the photoreceptor cell reduces its neurotransmitter output in response to absorption of light. This process is self-limited as the membrane complex transducin catalyzes GTP back to GDP, restoring the cell's tonic neurotransmitter release.

The excitatory "on" and "off" inputs to a ganglion cell are arranged to form an antagonistic center-surround receptive field. The action potential firing rate of an "on-center" ganglion cell is highest when a light stimulus is in the center of the receptive field with surrounding darkness. The action potential firing rate of "off-center" ganglion cells is highest when a light stimulus is in the peripheral receptive field, but not its center. When there is uniform illumination throughout a ganglion cell receptive field, the center and surround responses cancel each other and do not create an action potential.

Ganglion cell axons travel through the optic nerve and partially decussate in the chiasm, bringing together corresponding inputs from each eye. Some inputs follow pathways to mediate pupil light reflexes and circadian rhythms. The majority of inputs travel to the lateral geniculate nucleus. Different types of ganglion cells comprise separate pathways that are named for their targets in

the LGN of the thalamus. The three main types of ganglion cells are midget cells, which form the "P" (parvocellular) pathway; parasol cells, which form the "M" (magnocellular) pathway; and small bistratified ganglion cells, which form the "K" (koniocellular) pathway.

The chiasm is the site of decussation for axons from the optic nerve. This decussation serves to bring together information from the halves of each retina that view the same portion of the visual field. Axons from nasal ganglion cells cross and join axons from temporal ganglion cells from the contralateral eye. There is a greater number of crossed (53%) than uncrossed (47%) fibers.

Each optic tract contains axons from the ipsilateral temporal retina and the contralateral nasal retina. In the posterior tract, these axons fan out toward the LGN and interdigitate into its separate layers.

The number of cells in the LGN is large, with almost a 1:1 ratio to ganglion cell inputs. The hilum (central portion) of the LGN represents the macular vision. The superior visual field is represented in the lateral horn, and the inferior visual field is represented in the medial horn. The LGN is arranged in six neuronal layers, each with monocular inputs. Ganglion cell axons from the ipsilateral eye synapse in layers 2, 3, and 5. Axons from the contralateral eye synapse in layers 1, 4, and 6. Layers 1 and 2 contain the magnocellular layers which receive parasol ganglion cell inputs. Layers 3–6 contain parvocellular neurons and receive midget ganglion cell inputs. Scattered under each of the six major layers are the koniocellular cells.

The LGN is a relay station with dynamic control upon the amount and nature of information that is transmitted to the visual cortex. The pulvinar is another thalamic nucleus that forms a higher-order relay receiving descending cortical projections from both layers 5 and 6 of the visual cortex. The pulvinar nucleus is capable of modifying transmission in accord with requirements of selective visual attention.

The superior colliculi play a role in generating orienting eye and head movements to sudden visual stimuli. They are located in the dorsal midbrain within the tectal plate.

The pretectal nuclei receive a portion of fibers in the optic tract, which subserve the pupillary light reflex. There is consensual innervation to both pretectal nuclei, and each nucleus has dual connections to each Edinger-Westphal nucleus.

The suprachiasmatic nucleus (SCN) receives light information from a type of retinal ganglion cell that contains the photopigment melanopsin and demonstrates an intrinsic responsiveness to light. This allows the SCN to monitor ambient light levels reliably. The SCN communicates with the pineal gland, where melatonin secretion drives circadian rhythms.

Second-order neurons of the visual pathway form the optic radiations traveling from the LGN to the striate cortex in the occipital lobe. These neurons travel in two major groups: the temporal radiations termed Meyer's loop and the parietal radiations. Temporal radiations represent the contralateral homonymous superior field, and parietal radiations represent the contralateral homonymous inferior field.

The optic radiations arrive at the mesial surface of the occipital lobe, in the striate cortex. The parietal radiations synapse in the superior bank of calcarine cortex, while those from the temporal radiations arrive in the inferior bank. These axons make connections in cortical layer 4, which is termed the "stripe of Gennari." Macular projections make their synapses in the posterior pole of calcarine cortex. The macular representation is greatly magnified in the visual cortex retinotopic map; 2% of the visual field encompasses 60% of the striate cortex. This cortical magnification correlates to extremely high central acuity.

Cross-References

- ▶ Optic Nerve (Cranial Nerve II)
- ▶ Optic Tract
- ▶ RAPD (Relative Afferent Pupillary Defect)

Further Reading

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Aflibercept

► Antivascular Endothelial Growth Factor

After Cataract

► Capsular Bag Opacification

Afterimages

► Palinopsia

AGel Amyloidosis

► Meretoja Syndrome

Age-Related Macular Degeneration

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Synonyms

Age-related maculopathy (ARM); AMD; ARMD

Definition

Degenerative process of the choriocapillaris-retinal pigment epithelium (RPE) complex which leads to a significant loss in visual acuity.

Epidemiology

Age-related macular degeneration (AMD) is the leading cause of significant irreversible loss in visual acuity in people over 50 years old in developed countries. The prevalence increases with age, namely, from 1.6% in the age group 52–64 years to 28% in the age group 75–86 years. Pathologic features related to AMD may be found in the outer retina, retinal pigment epithelium (RPE), Bruch's membrane, and choriocapillaris. According to these abnormal findings, AMD may be classified as non-neovascular or neovascular, with a prevalence of 85–90% and 10–15%, respectively.

Histopathology and Clinical Features

Non-neovascular (Dry) AMD

The hallmark of the non-neovascular AMD is drusen. Other characteristic features are abnormalities of the RPE and choriocapillaris. The advanced form of this disease is geographic atrophy, characterized by atrophy of the outer layers of the retina and RPE with loss of choriocapillaris.

Drusen are small, yellowish white lesions located below the RPE. There are several types of drusen – hard, soft, basal laminar, and crystalline.

Hard Drusen

Hard drusen are smooth-surfaced, dome-shaped structures, located between the RPE and Bruch's membrane. They contain hyaline material, mucopolysaccharides, and lipids. These drusen are smaller than 50 mm in diameter. They are common in young adults and do not lead to macular degeneration.

Soft Drusen

Soft drusen are pale yellow lesions with poorly defined edges. They are a localized detachment of RPE with basal linear deposits (located external to the RPE, composed of an electron dense, lipid-rich material) or with basal laminar deposits (located between the plasma and the basement membranes of the RPE, composed of granular material with wide spaced collagen). They gradually enlarge to form a confluent drusen (contiguous boundaries between drusen). Soft drusen are classified into small (<63 μm), intermediate (63–125 μm), and large (>125 μm). The risk of progression from non-neovascular AMD to neovascular AMD increases with the size and the total area covered by drusen.

Basal Laminar Drusen

Basal laminar drusen are tiny and white, located between the plasma membrane and basement membrane of the RPE, mainly composed of collagen, laminin, and fibronectin.

Crystalline Drusen

Crystalline drusen are dehydrated soft drusen that may predispose to geographic atrophy.

Geographic Atrophy (GA)

GA is the advanced form of non-neovascular AMD, frequently associated with loss of central vision. GA is a well-demarcated area of decreased retinal thickness, which allows visualization of choroidal vessels. There is a loss of RPE cells in the area of atrophy with secondary loss of external neuro-retinal layers. The choriocapillaris may also be absent due to the RPE atrophy. GA typically develops in the eyes with drusen. As drusen fade, focal areas of atrophy may develop in their place; as they expand, GA is formed.

Differential Diagnosis

Differential diagnosis includes, from the most common to less frequent conditions, ▶ central serous chorioretinopathy (CSC), → pattern dystrophy, → cuticular drusen, and → drug toxicity (e.g., chloroquine toxicity.

Neovascular (Wet) AMD

Patients present with complains of sudden or gradual onset decrease in visual acuity, metamorphopsia, and central or paracentral scotomas.

The hallmark of the neovascular AMD is choroidal neovascularization (CNV).

The major clinical features include subretinal fluid (SRF), subretinal hemorrhage, sub-RPE fluid, sub-RPE hemorrhage, hard exudates, serous pigment epithelial detachment (PED), and fibrovascular PED. The overlying retina may show cystoid macular edema (CME).

Choroidal Neovascularization (CNV)

Any disturbance of Bruch's membrane can increase the likelihood that a break will occur, allowing choroidal vessels to grow into that place between the RPE and Bruch's membrane, between the retina and RPE, or a combination of both. Disciform scar represents the end stage of neovascular AMD.

The CNV may be visible as an area of grayish greenish color. Chronic neovascular AMD is characterized by subretinal fibrosis. The location of the CNV is divided into subfoveal (0 μm from foveal avascular zone (FAZ)), juxtafoveal (1–199 μm from FAZ), and extrafoveal (200–2,500 μm from FAZ).

The pathogenesis of CNV is not fully understood. It is generally agreed that angiogenic factors such as VEGF have a primary role in the initiation and growing of CNV.

Pigment Epithelial Detachment (PED)

PED is the result of a process by which the RPE separates from the underlying Bruch's membrane due to the presence of blood, serous exudate, drusen, or a neovascular membrane. PED appears as a smooth, dome-shaped subretinal elevation, with sharply demarcated. The pathogenesis of PED formation is incompletely understood, but most likely it involves penetration of CNV through Bruch's membrane into the sub-RPE space with secondary extravasation of fluid or blood and an increase in hydrostatic pressure that separates the RPE from the underlying Bruch's membrane. Hemorrhage or exudates

may or may not be presented, depending on the presence or absence of associated CNV.

Disciform Scar

An area of subretinal fibrosis or sub-RPE fibrosis. On examination it appears as dull, white fibrous tissue. It can present concomitantly with CNV or replace the latter over time. CNV is accompanied by fibroblasts, resulting thus in a fibrovascular complex that proliferates within the inner aspect of Bruch's membrane. This fibrovascular complex can disrupt and destroy the normal architecture of the choriocapillaris, Bruch's membrane, and the RPE. In addition, fibroglial and fibrovascular tissue can also disrupt and destroy the normal architecture of the photoreceptors and remaining outer retina. Ultimately, this process results in a disciform fibrovascular scar that replaces the normal architecture of the outer retina and leads to permanent loss of central vision.

Differential Diagnosis

Differential diagnosis includes, from the most common to less frequent pathologies, CNV caused by other conditions (i.e., ocular histoplasmosis syndrome, pathologic myopia, choroidal rupture, ▶ angioid streaks, or idiopathic), → polypoidal choroidal vasculopathy, and → choroidal tumors.

Genetics

AMD is a multifactorial disease; there are several known genes thought to be involved, including complement-related genes such as complement factor H, factor B, complement component 2, and complement C3. Other genetic factors that increase the risk for AMD include chromosome 10q26, inflammatory genes CXCR1 and TLR4, extracellular matrix fibulin, CST3, and MMP-9, and other genes that are involved include LPR6, VEGF, VLDRL, ACE, MnSOD, and EPHX1.

Risk Factors

- Age – the strongest risk factor.
- Race – Caucasian race is a risk factor.
- Heredity.
- Cigarette smoking.
- Possible risk factors include female gender, higher level of education, light iris color, hyperopic eyes, cardiovascular disease, hypertension, dyslipidemia, sunlight exposure, dietary fish intake, and alcohol consumption.
- Not associated with AMD – diabetes.

Imaging

Fluorescein Angiography (FA)

FA plays a critical role in the diagnosis and management of AMD. In the past FA was crucial in localizing and guiding both laser and photodynamic therapy (PDT). Nowadays, FA is useful in confirming the cause of exudative findings.

Patterns in non-neovascular AMD:

- Hard drusen appears as hyperfluorescent spots due to a transmission defect resulting from RPE thinning over the surface of the drusen. FA often reveals a greater number of hard drusen that can be seen clinically.
- Soft drusen form a shallow elevation of the RPE; thus during the early phase FA, there is a faint increasing hyperfluorescence of the drusen with no signs of leakage.
- Basal laminar drusen appears as a "starry sky," a multitude of tiny hyperfluorescent spots from multiple transmission defects.
- Focal hyperpigmentation appears as a blocked fluorescence on FA.
- GA does not hyperfluorescence in early phases due to loss of underlying choriocapillaris. In later phases there is a well-defined hyperfluorescence from staining of the exposed deep choroid.

Patterns in neovascular AMD:

- The angiographic appearance of CNV is governed by the density and maturity of the vessels and by the intervening tissue.
- Classic CNV is seen as a bright early hyperfluorescence lesion, almost immediate, and also has well-demarcated boundaries. This corresponds to a relatively acute growth of

vessels that break through Bruch's membrane and the RPE and then proliferative above the RPE in the subretinal space. There is prominent leakage and eventually the vessels and their borders become obscured by the leakage.

- Occult CNV is defined by a fibrovascular PED in which abnormal vessels remain beneath intact RPE. There are two types of occult CNV:
  - Fibrovascular RPE detachment is seen as a slowly increasing in fluorescence often in a heterogeneous manner. The dye retained in the fibrovascular PED and leakage from the fibrovascular PED can result in the appearance of hyperfluorescence inside the fibrovascular PED, subretinal space, or the retina.
  - In late leakage of undetermined source, there is no early hyperfluorescence, and during the late phase, there is generalized leakage beneath the RPE often either mild to moderate stippled fluorescence.
- Classic and occult CNV can occur in the same lesion. If the lesion is composed of 50% or more classic CNV, it is termed "predominantly classic"; if there is less than 50%, it is termed "minimally classic."

Indocyanine Green Angiography (ICGA)

ICGA is a useful technique for the diagnosis of AMD, especially in the presence of occult CNV. ICG allows better recognition of subtypes of occult CNV.

Patterns in ICGA:

- Serous PED – ICGA reveals a minimal blockage of normal choroidal vessels; thus a serous PED is hypofluorescent on ICG.
- Classic CNV has a similar appearance to that with FA, a bright early hyperfluorescence lesion.
- In occult CNV type 1, the ICGA reveals early vascular hyperfluorescence and late staining of the abnormal vessels.
- Occult CNV type 2 is associated with a serous PED of at least one disk diameter in size.
- Occult CNV is also subgrouped into two types, a solitary area of well-defined focal neovascularization (hot spot) and the other with a larger and delineated area of neovascularization (plaque).

Optical Coherence Tomography (OCT)

Provides cross-sectional retinal images that closely resemble to the histology. In non-neovascular AMD, OCT is able to track changes in drusen volume, morphology, and GA. In neovascular AMD, OCT can illustrate CNV, SRF, and CME. Qualitative and quantitative information provided by OCT are currently used in retreatment decisions:

Patterns in non-neovascular AMD:

- Drusen common pattern is convex and homogenous with internal reflectivity. The photoreceptor layer overlying drusen has shown to be significantly thinned.
- In GA there is an attenuation of the outer retina with loss of the external limiting membrane, the outer nuclear layer is thinned, and there is a posterior bowing of the outer plexiform layer. At the margin of atrophy, two kinds of patterns can be noted – smooth and irregular.

Patterns in neovascular AMD:

- Occult CNV appears as a localized fusiform PED which may be serous or fibrovascular in nature.
- Classic CNV can present as highly reflective fibrovascular tissue with irregular borders between the RPE and Bruch's membrane or above the RPE. It may also present as a localized serous or fibrovascular PED. Disruption of the photoreceptor layer or CME can be observed.
- In general, active CNV (of any type) is associated with the presence of fluid. The fluid can accumulate in the subretinal space, sub-RPE space, or between all layers of the inner retina.

Treatment

Neovascular AMD

Angiogenesis is characterized by a complex cascade of events. The first step in the cascade is vasodilation of existing vessels and increased vascular permeability. This is followed by degradation of the surrounding extracellular matrix, which facilitates migration and proliferation of endothelial cells. After endothelial cells proliferate, they join together to form a lumen, which becomes a new capillary. The vessels subsequently mature and undergo remodeling to form a stable vascular network. The successful execution of this cascade requires a carefully balanced interplay of growth-promoting and growth-inhibiting angiogenic factors. Identified activators of angiogenesis include vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF) families, transforming growth factor (TGF)-α and TGF-β, angiopoietin-l, and angiopoietin-2. Inhibitors of angiogenesis include thrombospondin, angiostatin, endostatin, and pigment epithelium-derived factor (PEDF). Most recent research has focused on VEGF.

VEGF is a homodimeric glycoprotein, which is a heparin-binding growth factor specific for vascular endothelial cells. It can induce angiogenesis, vascular permeability, and lymphangiogenesis. VEGF expression is increased in RPE cells during the early stages of AMD, suggesting that VEGF plays a role in the initiation of neovascularization rather than being secondary to it. In addition, high concentrations of VEGF have been observed in excised CNV from AMD patients as well as in vitreous samples from patients with CNV. There are four major VEGF isoforms: $VEGF_{121}$, $VEGF_{165}$, $VEGF_{189}$, and $VEGF_{206}$. $VEGF_{165}$ is thought to be the most pathologic.

Anti-VEGF Therapies

Pegaptanib is an aptamer that binds human $VEGF_{165}$ with high affinity and specificity. Pegaptanib selectively binds to the heparin-binding domain of $VEGF_{165}$ and larger isoforms, preventing ligand-receptor binding. Unfortunately, patients in general still lost vision with pegaptanib therapy, and the use of this drug has dropped as newer anti-VEGF agents have been developed.

Bevacizumab (Avastin) is a full-length humanized murine monoclonal antibody directed against human VEGF-A. Bevacizumab was approved by FDA for the intravenous treatment of metastatic colon cancer; intravitreal injection of bevacizumab is an off-label use.

Ranibizumab (Lucentis) is a recombinantly produced, humanized, antibody (Fab) fragment that binds VEGF. Unlike pegaptanib, ranibizumab binds to and inhibits the biologic activity of all active forms of VEGF-A and their active degradation products.

Aflibercept (Eylea, VEGF Trap-eye) is a recombinant chimeric VEGF receptor fusion protein in which the binding domains of VEGF receptors 1 and 2 are combined with the Fc portion of IgG to create a stable, soluble, high-affinity inhibitor. Aflibercept is designed to inhibit all members of the VEGF family (VEGF-A, VEGF-B, VEGF-C, and VEGF-D) and placental growth factors (PIGF-1 and PIGF-2). Aflibercept binds VEGF-A with a higher affinity than any other anti-VEGF drug.

Additional anti-VEGF drugs are in development.

Regimens of treatment:

- Pro re nata (PRN) or "treat and observe": patients are treated with a loading dose of three monthly injections, followed by as-needed decision to treat. Decision to treat is based on the presence of worsening BCVA, clinical evidence of disease activity on fundoscopy, or OCT evidence of retinal thickening in the presence of intraretinal fluid or SRF.
- "Treat and extend": initially, patients are treated with a loading dose of three monthly injections, and then the interval between injections is gradually increased, until stabilization of the neovascular AMD is achieved. The "treat and extend" is a dosing regimen designed to resolve all the intraretinal fluid

and SRF and to keep the macula "dry" as long as possible with less injections and visits than the monthly dosing.
- Monthly injections: patients are treated with monthly injections, regardless of BCVA, fundoscopy findings, or OCT evidence of retinal thickening in the presence of intraretinal fluid or SRF.
- With aflibercept, patients are treated with a loading dose of three monthly injections and then once every 2 months.

Non-VEGF Pathways

Although anti-VEGF therapies have dramatically improved treatment outcome, many patients still fail to improve in visual acuity. There are other cellular pathways that mediate or modulate angiogenesis, such as angiogenic signaling, endothelial migration, vessel maturation, and fibrosis. Each of these mechanisms can be harnessed or blocked in order to improve the therapeutic effect. In the future, a combined approach targeting multiple pathways is likely to be available.

Laser Photocoagulation

At present, anti-VEGF therapy is the first-line treatment for all subtypes of subfoveal CNV secondary to AMD. In the past, laser photocoagulation based on FA location of the CNV was the therapy of choice for several categories of well-defined CNV. A significant loss in visual acuity occurred over time in most laser-treated eyes.

Photodynamic Therapy (PDT)

PDT is a two-step process that entails systemic administration of a photosensitizing drug followed by the application of light of a particular wavelength to the affected tissue to incite a localized photochemical reaction. This reaction generates reactive oxygen species that can lead to capillary endothelial cell damage and vessel thrombosis. The FDA approved PDT with verteporfin for the eyes with predominantly classic CNV. Although PDT is an improvement over subfoveal laser, on average, patients still lose visual acuity and have minimal visual gain with monotherapy. With the advent of pharmacotherapy, PDT use has dropped considerably.

Non-neovascular AMD

In the Age-Related Eye Disease Study (AREDS), participants were stratified into four categories:

1. No drusen or few small drusen.
2. Extensive small drusen, pigment abnormalities, or at least one intermediate druse in at least one eye.
3. Extensive intermediate drusen, large drusen, or noncentral GA in at least one eye.
4. Advanced AMD or vision loss due to non-advanced AMD in one eye.

Patients were treated with high dose of micronutrient supplements consisting of antioxidants and vitamins (500 mg vitamin C, 400 IU vitamin E, and 15 mg beta-carotene) and zinc (80 mg zinc oxide and 2 mg cupric oxide to prevent zinc-induced anemia).

According to this study, the combination of antioxidant vitamins and zinc was protective against the development of advanced AMD for categories 3 and 4. Patients in categories 1 and 2 had a very low risk to develop advanced AMD.

AREDS-2 studied the effect of adding lutein, zeaxanthin, and omega-3 to the original formula. The study showed that removing the beta-carotene and lowering the zinc did not have an effect on the progression rate. Lung cancer rates were higher in the beta-carotene group, mostly in former smokers who had stopped smoking more than a year before. Lutein and zeaxanthin would be appropriate substitutes for beta-carotene, and they did not cause any increase in the risk of lung cancer. The addition of omega-3 did not reduce the risk of progression. The results led to the recommendation that the AREDS formula be adjusted by the removal of beta-carotene and addition of lutein and zeaxanthin.

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Age-Related Maculopathy (ARM)

► Age-Related Macular Degeneration

Agnosia, Object

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Synonyms

Visual agnosia; Visual form agnosia

Definition

A visual agnosia is the loss of ability to visually recognize formerly familiar objects, while there is no defect in vision nor is there any significant memory loss to account for the symptom. Two subtypes include apperceptive visual agnosia and associative visual agnosia. Patients with apperceptive visual agnosia display the ability to see contours and outlines when shown an object, but they experience difficulty if asked to categorize objects. Patients with associative visual agnosia experience difficulty when asked to name objects.

Etiology

Apperceptive visual agnosia is associated with damage to one hemisphere, specifically the posterior sections of the right hemisphere. Associative agnosia is associated with damage to both the right and left hemispheres at the occipitotemporal border.

Clinical Presentation

Patients with apperceptive visual agnosia are unable to distinguish visual shapes and have trouble recognizing visual stimuli and have difficulty with copying images. Patients with associative visual agnosia can describe visual scenes and objects but may fail to recognize them. These patients are typically still able to reproduce an image through copying.

Diagnostics

In order to assess a patient for agnosia, it must first be verified that the individual is not suffering from a loss of vision and that their language and cognitive functions are intact. Copying and matching tasks may help differentiate apperceptive agnosia (unable to match two stimuli that are identical in appearance) from associative agnosia

(unable to match different examples of the same stimuli).

Differential Diagnosis

Vision loss and cognitive degeneration.

Therapy

When possible, the underlying cause is treated (i.e., surgery for brain tumor). Patients with object agnosia may benefit from cognitive-perceptual rehabilitation. This therapy involves teaching the patient other ways to access information, bypassing the damaged pathways. This can include taking advantage of the patient's continued ability to recognize objects using alternate senses, such as taste, smell, touch, and hearing. Patients with visual agnosia often benefit from predictable environments and consistency in task stimuli.

Prognosis

Recovery may be influenced by the type, size, and location of the lesion causing the visual agnosia. Most recovery occurs within the first 3 months but may continue to a variable degree up to a year.

Cross-References

- ▶ Akinetopsia
- ▶ Alexia, Without Agraphia
- ▶ Parietal Radiations Lesion
- ▶ Temporal Radiations Lesion

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AICA

▶ Anterior Inferior Cerebellar Artery

AIDS and Neuro-Ophthalmology Manifestations

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Definition

Neuro-ophthalmic problems are known to occur both in human immunodeficiency virus (HIV) infection and acquired immune deficiency syndrome (AIDS). Central nervous system (CNS) opportunistic infections and malignancies such as lymphoma are the major source of these AIDS-related manifestations, but some are the result of direct effect of HIV on the CNS. Neuro-ophthalmic signs may in fact be the initial manifestation of AIDS.

Optic neuropathy in patients with HIV/AIDS may result from inflammation, ischemia, infection, compression, infiltration, and increased

intracranial pressure (ICP). Inflammation results largely from opportunistic infections. However, the optic nerve may be a direct site of insult of the HIV virus. Primary HIV optic neuropathy however is a diagnosis of exclusion. It may present clinically as papillitis, retrobulbar optic neuritis, or neuroretinitis. Visual loss is variable. Early initiation of highly active antiretroviral therapy (HAART) has been shown to improve vision in some cases. Infectious optic neuropathy may be caused by cytomegalovirus (CMV), toxoplasmosis, herpes simplex virus (HSV) and herpes zoster virus (HZV), syphilis, tuberculosis, and *Cryptococcus neoformans*.

CMV can involve the optic nerve during advanced stages of CMV retinal disease, leading to severe vision loss. Furthermore, this infection carries a poor prognosis because of often irreversible necrosis of the optic disk. Treatment includes high doses of intravenous foscarnet and/or ganciclovir and also with oral valganciclovir.

Toxoplasma optic neuritis can present as papillitis, retrobulbar optic neuritis, and neuroretinitis often with retinochoroiditis.

HSV and HZV may produce acute retinal necrosis (ARN) and progressive outer retinal necrosis (PORN) in patients with AIDS. Disk edema, hyperemia, and atrophy may be seen. Intravenous acyclovir is the first line of treatment.

Syphilitic optic neuritis may present with papillitis, retrobulbar optic neuritis, neuroretinitis, and optic perineuritis. Visual outcomes with treatment remain variable.

Cryptococcus neoformans optic neuritis can produce papillitis, retrobulbar optic neuritis, and optic perineuritis. Prompt administration of intravenous amphotericin b and 5-flucytosine before permanent nerve damage develops may preserve vision, and serial spinal taps to reduce increased ICP may be necessary to treat cryptococcal papilledema.

Optic neuritis has also been reported with mycobacterium tuberculosis, histoplasmosis, hepatitis B, and *Bartonella henselae*. Papilledema may develop in AIDS patients from raised intracranial pressure from CNS infections or neoplastic processes. Optic nerve sheath fenestration has been used to preserve vision in cases of papilledema (e.g., cryptococcal meningitis).

Visual field defects in HIV may be due to optic neuropathy, and retrochiasmal pathways produce homonymous hemianopia and have resulted from toxoplasmosis, cryptococcosis, cerebral astrocytoma, neurosyphilis, tuberculosis, progressive multifocal leukoencephalopathy, and lymphoma. Cortical blindness and visuospatial abnormalities could result from involvement of the primary or association visual cortices.

Ocular dysmotility in HIV/AIDS can result from nuclear, supranuclear, or infranuclear lesions causing cranial nerve palsies, gaze palsies, internuclear ophthalmoplegia, and nystagmus. Rarely, these symptoms may be the presenting features of HIV/AIDS.

Chronic progressive external ophthalmoplegia-like syndromes may occur in patients with long-standing HIV infection, especially those who have received long-term treatment with HAART Sudhakar et al. (2012).

Pupillary abnormalities seen in HIV/AIDS include RAPD, light-near dissociation tonic pupil, iris abnormalities, and Horner syndrome.

Cross-References

- ▶ Bartonella henselae, Cat Scratch
- ▶ Retinitis Pigmentosa, Decreased Vision in Neuro-Ophthalmology
- ▶ Optic Neuritis

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Akinetopsia

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Synonyms

Cerebral akinetopsia; Motion blindness

Definition

An inability to perceive motion in the visual field.

Etiology

Akinetopsia is caused by a lesion in area MT/V5 of the extrastriate cortex. It can also be caused as a side effect of certain antidepressants or due to damage by stroke or Alzheimer disease.

Clinical Presentation

Patients state that their worlds are devoid of or have impaired motion perception. They are able to see stationary objects but cannot perceive moving objects. Generally the faster an object moves, the more difficult it is to see. Visuomotor tasks such as reaching for objects and catching objects may also be disturbed. These patients typically maintain normal spatial acuity, flicker detection, stereopsis, and color vision.

Diagnostics

Basic visual functions should be tested before a patient's symptoms are ascribed to akinetopsia. An examination of visual acuity, spatial contrast sensitivity, and visual fields may be done. General intellect may be measured using the Wechsler Adult Intelligence Scale-Revised (WAIS-III). Testing of motion perception may be done using random dot cinematograms (RDCs). RDCs present a motion signal against a spatially random background and can be designed to test different aspects of motion perception. This is currently generally available only in research settings. It may also be possible to assess motion vision by observing smooth pursuit or optokinetic eye movements.

Differential Diagnosis

Vision loss, cognitive degeneration.

Therapy

There is currently no effective treatment or cure for akinetopsia. In cases of akinetopsia caused as a side effect of antidepressants, vision returns to normal after discontinuation of the drug.

Cross-References

▶ Agnosia, Object
▶ Alexia, Without Agraphia

► Parietal Radiations Lesion
► Temporal Radiations Lesion

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Alagille-Watson Syndrome (AWS)

► Arteriohepatic Dysplasia (Alagille Syndrome), Retinal Degeneration

Albinism

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Synonyms

Ocular hypopigmentation; Nystagmus

Definition

Albinism is a genetic impairment of melanin production (melanogenesis) characterized by congenital hypopigmentation of the eyes, skin, and hair (oculocutaneous albinism, OCA) or of the eyes alone (ocular albinism, OA). The inheritance pattern of these conditions is different. OCA has an autosomal recessive transmission, whereas OA is X-linked recessive.

Etiology

In albinism there is complete or partial deficiency of melanin, which is responsible for the natural pigmentation of the skin, hair, and eyes. Melanin is normally produced in the melanosome, an intracellular organelle of melanocytes, which are derived from two embryonic tissues: the neural crest and optic cup. Melanocytes originating from the neural crest are present in the skin (epidermal-dermal junction), hair follicles, and eyes (choroid and iris stroma), whereas melanocytes of the retinal pigment epithelium are derived from the neuroectoderm of the optic cup. Melanin is produced from the amino acid tyrosine. The most important step in this conversion is catalyzed by the enzyme tyrosinase.

Clinical Presentation

The external features of albinism are readily noticeable and include: white skin, white hair, and pink-blue eyes. Ocular features include absence of pigment in the uveal tract and retinal pigment epithelium causing iris transillumination defects and prominence of choroidal vessels, macular hypoplasia, optic nerve hypoplasia, and abnormal retino-cortical projections characterized by increased decussation of optic nerve fibers in the optic chiasm. Reduced visual acuity, nystagmus, photophobia, strabismus, and high astigmatic refractive errors are typically present.

Oculocutaneous Albinism

OCA is characterized by inherited hypopigmentation of the skin, hair, and eyes with an estimated inheritance frequency of 1:28,000 affecting both Caucasians and Blacks. It is classified into three subtypes, designated as OCA 1, OCA 2, and OCA 3. The inheritance pattern of all three subtypes is autosomal recessive.

OCA 1 (OMIM #203100) is tyrosinase-negative OCA. It is caused by a homozygous or compound heterozygous mutation in the tyrosinase gene (*TYR*) on chromosome 11q14. It is divided into two subtypes: OCA 1A (classic tyrosinase-negative OCA) in which there is complete absence of tyrosinase activity and OCA 1B in which there is some degree of residual tyrosinase activity. Patients with OCA 1A have no

capability of producing any melanin during their lifetime or following sun exposure, whereas patients with OCA 1B have no skin, hair, and eye pigmentation at birth, but they can produce some melanin later on in life, causing their skin and hair to mildly darken with age. They can also mildly tan on sun exposure.

OCA 2 (**OMIM** #**203200**) is tyrosinase-positive OCA. This subtype is caused by mutations of the P gene, mapped to chromosome 15q11. This is the most common type of OCA and it has a wide range of phenotypic expression. Although complete absence of melanin pigment is usually present in birth, most patients with OCA 2 acquire small amounts of pigment with age. In Caucasians the skin is typically white and does not tan on sun exposure, the hair is blonde, and the eyes are pink-blue with iris transillumination defects, depending on the degree of iris pigmentation. In Blacks the skin is creamy-white and does not tan and the eyes are blue-gray. Individuals with OCA 2 have the same ocular features of OCA 1, including reduced visual acuity and nystagmus; however, they are typically less severe.

OCA 3 (**OMIM** #**203290**) is caused by homozygous or compound heterozygous mutation in tyrosinase-related protein-1 (*TYRP1*) gene on chromosome 9p23. When first found in Southern African Blacks, it was named "rufous (red) oculocutaneous albinism (ROCA)," because it is characterized by bright copper-red coloration of the skin and hair and dilution of the color of the iris. This subtype is present only in Africans or African American individuals, and some of them do not have the classic features of albinism, such as iris translucency or foveal hypoplasia.

Oculocutaneous Albinism Associated with Systemic Disease

Hermansky-Pudlak syndrome 1 (**HPS1**, **OMIM** #**203300**) is a rare autosomal recessive disorder, caused by homozygous or compound heterozygous mutation in the *HPS1* gene on chromosome 10q24. This syndrome is characterized by the triad of OCA, bleeding, and lysosomal ceroid storage resulting from defects of multiple cytoplasmic organelles: melanosomes, platelet-dense granules, and lysosomes. This syndrome occurs primarily in Puerto Rican individuals, where the estimated frequency of the gene defect is 1:1800. The clinical features of HPS1 include the typical ocular manifestations of OCA accompanied by bleeding diathesis and easy bruisability caused by defective platelet function without a reduction in their counts. The skin is creamy white with some tanning possible on sun exposure. Freckles in sun-exposed areas and pigmented nevi are frequently found. Interstitial pulmonary fibrosis and renal failure are commonly present as a result of the lysosomal storage dysfunction. **Hermansky-Pudlak syndrome 2** (**HPS2**, **OMIM** #**608233**), which includes immunodeficiency in its phenotype, is caused by mutation in the *AP3B1* gene on chromosome 5q14. Other **Hermansky-Pudlak syndromes** (**HPS3 to HPS9**) caused by different gene mutations and a similar phenotypic expression to HPS1 have been found in recent years.

Chediak-Higashi syndrome (**OMIM** #**214500**) is caused by homozygous or compound heterozygous mutation in the lysosomal trafficking regulator *(LYST)* gene on chromosome 1q42. It is characterized by hypopigmentation of the hair and eyes (partial albinism) and increased susceptibility to infection and lymphoreticular malignancies. Large eosinophilic, peroxidase-positive inclusion bodies are present in leukocytes, and neutropenia is frequent. Death often occurs before the age of 7 years.

Ocular Albinism

Ocular albinism type 1 (**OMIM** #**300500**) is the most common form of ocular albinism, caused by a mutation in the *GPR143* gene, mapped to chromosome Xp22. Affected Caucasian males have the ocular features of albinism, including decreased visual acuity, nystagmus, iris hypopigmentation, and macular hypoplasia, with a normally pigmented skin and hair. In contrast to Caucasians, affected Black males can have brown irides with little or no translucency and varying

degrees of fundus hypopigmentation, the so-called nonalbinotic fundus. Heterozygote carrier females usually have punctate iris translucency and a mottled pattern of fundus pigmentation as a result of X chromosome inactivation (lyonization). It is thought that the OA1 protein has a regulatory role in distributing melanosomes between microtubule- and actin-based cytoskeletal elements and its deficiency results in formation of giant macromelanosomes in ocular and skin melanocytes.

Lab Diagnostics

Prenatal diagnosis of albinism is possible.

The degree of tyrosinase activity in hair bulb culture differentiates between OCA 1 (tyrosinase negative) and OCA 2 (tyrosinase positive).

In recent years, optical coherence tomography has been found to be useful for demonstrating foveal hypoplasia in patients with albinism (Izquierdo et al. 2007). Visual evoked potential (VEP) in albinism is typically asymmetric (Russell-Eggitt et al. 1990). Monocular flash stimulation elicits a greater response in the contralateral occipital cortex because 90% of optic nerve fibers cross in the optic chiasm to reach the opposite lateral geniculate nucleus and visual cortex. The asymmetrical VEP and normal Electroretinography (ERG) recorded in infants and young children with albinism permits distinction of this disease from other conditions with whom they may be confused by a clinical examination only, including congenital cone dysfunction and infantile nystagmus syndrome.

Management

Efforts in albinism are made to improve vision with appropriate refractive correction and low-vision aids. Tinted lenses can provide relief from photophobia and glare, and protection from ultraviolet light exposure is also important. Strabismus surgery can be performed when strabismus causes a significant concern (Wright and Strube 2012).

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Alexander's Law

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Definition

Alexander's Law states that nystagmus is often increased with the eyes directed toward the fast-phase direction (e.g., downbeat nystagmus is worse in downgaze) compared to the slow-phase direction. This phenomenon occurs frequently in individuals who have an acute peripheral or central vestibular lesion.

It has been proposed that Alexander's Law is an attempt made by the nervous system to

compensate for vestibular lesions that occurs via two different mechanisms. First, there is a gaze-independent component, which is influenced by the vestibulo-ocular reflex. The second component is a gaze-dependent nystagmus which is from unilateral inhibition on the neural integrator. On physical exam, this phenomenon can be reduced by visual fixation.

Further Reading

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Alexia, Without Agraphia

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Synonyms

Disconnection syndrome; Pure alexia; Pure word blindness; Word blindness

Definition

Alexia without agraphia is an acquired inability to comprehend written language as a consequence of brain damage. It is a disorder of written language. A specialized variety of aphasia, this term alexia without agraphia refers to a specific disability in reading where the ability to write is preserved. There may be intact auditory and verbal aspects of language but there is a loss of efficient reading despite adequate visual acuity. It was first described by Dejerine in a patient with an associated incomplete right homonymous hemianopia from a lesion of the left fusiform and lingual gyri. The left angular gyrus stores the visual representation of words (needed for reading and writing), and a disconnection of the visual inputs crossing in the splenium of the corpus callosum of one hemisphere (typically the intact right occipital lobe) from the left angular gyrus could disrupt reading but leave writing intact.

Etiology

The most common cause of this syndrome is ischemic or thromboembolic disease; however, it had also been reported with transtentorial herniation and intra- or extraaxial left occipital region neoplasms (e.g., primary or metastatic tumor, cerebral abscess, demyelinating plaque, vascular malformation, traumatic shear hemorrhage, etc.). Of note it had been also reported with carbon monoxide poisoning and in migraine. Theoretically, any process that affects the splenium of the corpus callosum and related white matter tracts can result in this disconnection syndrome:

- In the case of damage to the left visual cortex and the splenium, words perceived in the right visual cortex are unable to cross over to the language areas in the left angular gyrus and patients will have diminished ability to read.
- Thus, the clinical syndrome of alexia without agraphia is typically due to combined lesions of left occipital lobe and splenium of the corpus callosum and is often caused by ischemic lesions in the distribution of the left posterior cerebral artery.

Clinical Presentation

The key clinical feature is the dissociation between the inability to read and normal writing performance. Patients can write fluently and spontaneously, but typically cannot read what they have written. The disease has a wide range of difference in the clinical presentation which ranges from the milder form in which reading is slow and effortful to the complete lack of reading ability. Words may be read one letter at a time, creating a characteristic "word length effect" with prolonged naming latencies with increasing numbers the number of letters in the word being read. This is referred to as letter-by-letter reading, or spelling dyslexia. On the other hand, in the severe form (global alexia), patients cannot read words or letters or even musical notations or map symbols (i.e., visuographemic alexia).

The ability to name objects may be preserved, and patients with the pure syndrome can recognize objects by using other modalities (e.g., auditory, taste, smell, or even by touch or texture). Spelling and spelling comprehension are typically normal. Theoretically writing should be normal or nearly so; however, subtle defects can usually present (e.g., letters are too large or too widely spaced, an absence or misuse of punctuation, misplaced or inappropriate use of capitals, letters dropped or reduplicated). The syndrome can be seen with acalculia as well.

Pure alexia is often part of a triad: right homonymous visual field defect (from left occipital involvement) and there may be color anomia (impaired naming of colors) or right hemiachromatopsia. Rarely, pure alexia can occur without the hemianopia.

To summarize the clinical criteria for the diagnosis of pure alexia:

1. Severe disturbance of reading comprehension (alexia).
2. Intact and correct writing.
3. Normal oral spelling.
4. Right homonymous hemianopia.
5. Color anomia or hemidyschromatopsia.
6. Verbal amnesia may or may not be present.

Diagnostics

The diagnosis is based on physical examination and detailed language and mental state examination. The laboratory tests required depend on the underlying pathophysiology. Neuroimaging is required to localize and diagnose the cause. Contrast-enhanced cranial CT and MRI are the mainstays of neuroimaging. Neuropsychological testing and speech therapy evaluation may be helpful.

Differential Diagnosis

1. Alexia with agraphia
2. Paralaxia
3. Visual agnosia
4. Amnesia
5. Global aphasia
6. Conduction aphasia
7. Expressive aphasia
8. Receptive aphasia
9. Pure word deafness
10. Thalamic aphasias
11. Subcortical aphasias
12. Transcortical aphasias
13. Right hemisphere language disorders

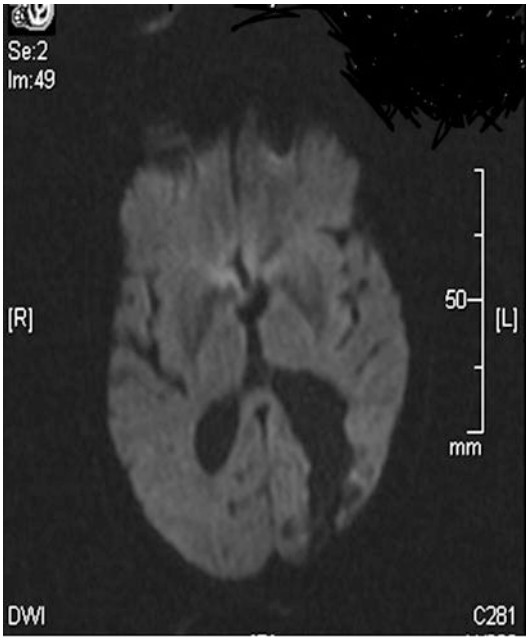
Prophylaxis

NA

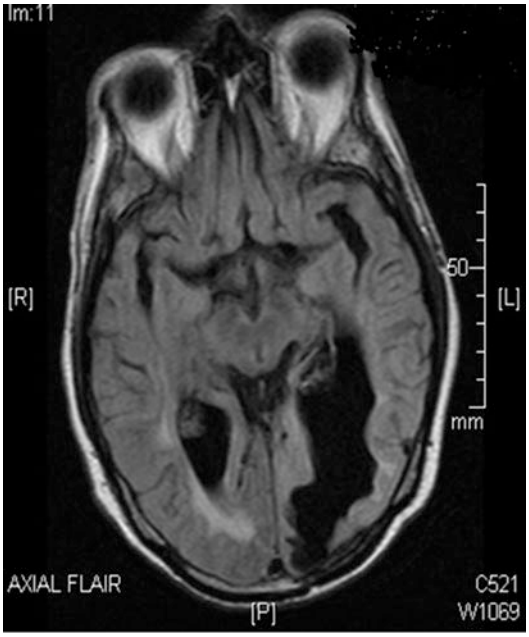
Therapy

The treatment of a patient with depends on the cause of the alexia, without agraphia, e.g., acute stroke, tumor, or infections. Speech and language therapy is the mainstay of care for patients with alexia, without agraphia.

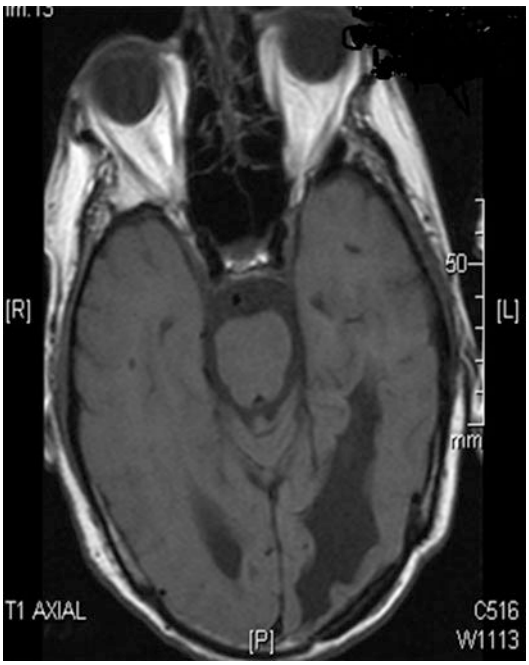
The use of remediation program consists of training by head turning to compensate for a right homonymous hemianopia visual field defect, letter-by-letter reading out loud, practice in naming objects, and drill with flash cards. Speech and language therapy may improve clinical outcome, and psychological support is



Alexia, Without Agraphia, Fig. 1 Cranial diffusion weighted imaging (DWI)



Alexia, Without Agraphia, Fig. 3 T2-fluid attenuation inversion recovery (FLAIR) sequence axial MRI (Figure 3) show an area of encephalomalacia in the left occipital cortex corresponding to the clinical symptoms of alexia without agraphia in a patient with a right complete homonymous hemianopsia after remote occipital stroke



Alexia, Without Agraphia, Fig. 2 Axial T1-weighted magnetic resonance imaging (MRI)

important but there is no clear benefit of medical treatment (e.g., dopaminergic, cholinergic, and stimulant drugs) (Figs. 1, 2, and 3).

Prognosis

Epidemiology

NA

Cross-References

- ▶ Idiopathic Facial Paralysis
- ▶ Pure Word Blindness
- ▶ Visual Agnosia

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Allergic Conjunctivitis

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Synonyms

Conjunctivitis; Eye allergies; Ocular allergies; Perennial allergic conjunctivitis; "Pink eye"; Seasonal allergic conjunctivitis

Definition

Inflammation of the conjunctiva due to allergic exacerbation (Bielory and Friedlaender 2008)

Etiology

Allergic conjunctivitis is caused by external allergens that come into contact with the eye (Haq et al. 2012). Allergens can include environmental exposure or medications applied directly to the eye. Examples include pollen, dusts, molds, spores, animal dander, cosmetics, industrial chemicals, eye drops (e.g., artificial tears), glaucoma drops, and ointments.

Allergic conjunctivitis can present acutely, seasonally, or perennially.

Acute presentations are triggered by a transient presentation of an allergen, e.g., animal dander. Symptoms tend to resolve within 24 h of allergen removal (Bielory and Friedlaender 2008).

Seasonal forms tend to coincide with pollen seasons varying with geography. Seasonal conjunctivitis is the most common type and typically occurs during the spring and summer months, with increased levels of airborne environmental allergens.

Perennial allergic conjunctivitis tends to display mild, chronic symptoms that are linked to long-standing allergens, such as animal dander, dust, or molds.

Clinical Presentation

Common presentations are sudden onset of itchy eyes and eyelids, foreign body sensation, watery/mucoid discharge, glassy chemosis, burning, and hyperemia (Haq et al. 2012). Symptoms tend to be bilateral and are not accompanied by pain. It is also often seen as a triad of conjunctivitis, rhinitis, and wheezing (Bielory and Friedlaender 2008). Visual acuity, pupil response, and intraocular pressure remain typically unaffected. Acute viral or bacterial conjunctivitis may present with similar symptoms, however, with more profuse and purulent discharge.

Patients with allergic conjunctivitis may have history of asthma, eczema, or allergies.

Diagnostics (Lab Diagnostics)

Allergic conjunctivitis is a clinical diagnosis. Blood tests or skin tests are not required unless needed in some patients.

Differential Diagnosis

Differential diagnosis includes infectious conjunctivitis, blepharitis, dry eye, microbial keratitis, iritis, and acute glaucoma.

Prophylaxis

Avoidance of known environmental or medical allergens helps to prevent symptom onset (Ono and Abelson 2005).

Patients experiencing frequent attacks (more than 2 days per month) may require prophylactic therapy with topical medicine containing both antihistamine and mast cell stabilizer properties. Efficacy should be assessed after 2 weeks of therapy.

For seasonal/perennial allergic conjunctivitis, prophylactic treatment 2–4 weeks before expected onset of symptoms is recommended.

Therapy

Acute Allergic Conjunctivitis

1. Allergen avoidance.
2. Cold compress to reduce mild symptoms.
3. Treatment if necessary. Combination therapy has been found to be effective in reducing symptoms (Ono and Abelson 2005).

Topical antihistamines are recommended to reduce symptoms of itchiness and watering. Examples include levocabastine, emedastine, and olopatadine

Oral antihistamines are recommended if symptoms persist. However, topical agents are preferred due to fast-acting and fewer side effects.

Examples include fexofenadine, loratadine, and cetirizine.

Vasoconstrictors reduce redness and edema; however, regular use for more than 2 weeks can lead to rebound hyperemia. Short-term or episodic treatment is recommended. Examples include naphazoline-pheniramine and naphazoline-antazoline.

Mast cell stabilizers reduce inflammatory response from mast cells. The effects of these medications last longer than antihistamines. Examples include lodoxamide and nedocromil.

Seasonal/Perennial Allergic Conjunctivitis

1. Prophylactic treatment for expected symptom onset
2. Similar treatment as acute allergic conjunctivitis

Additional therapies for refractive conjunctivitis include immunotherapy, corticosteroids, and topical NSAIDs (e.g., ketorolac). Corticosteroids and topical NSAIDS should be monitored and used only when other medication trials have failed to produce results.

Prognosis

Allergen avoidance provides excellent prognosis for acute allergic conjunctivitis (Ono and Abelson 2005).

Recurrence of seasonal allergic conjunctivitis symptoms occurs annually, though symptom severity may decline after age 50.

Epidemiology

Allergic conjunctivitis affects about 20% of the population annually (Bielory and Friedlaender 2008). Allergic conjunctivitis typically appears in young adults with average age of onset at 20 years. Roughly half of patients also have a personal or family history of allergies, such as asthma, eczema, or allergic rhinitis.

Cross-References

- ▶ Blepharitis
- ▶ Crystalline Keratopathy, Infectious
- ▶ Dry Eye
- ▶ Iridotomy
- ▶ Keratitis

References

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Allergic Dermatitis

- ▶ Contact Dermatoblepharitis

Allograft Rejection

► Subepithelial Graft Rejection

Alport Disease/Syndrome, Renal

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Definition

Oculo-auditory-renal syndrome comprising of glomerulonephritis, sensorineural hearing loss, and ocular findings.

Etiology

Alport syndrome results from a genetic mutation in one of three genes, COL4A3, COL4A4, or COL4A5 encoding for the collagen α3α4α5(IV) found in the basement membranes of the eye (cornea, lens, retina/RPE), cochlea, and glomerulus. Most commonly, the inheritance pattern is X-linked dominant (Xq22.3; COL4A5), although autosomal recessive and rarely autosomal dominant inheritance has been described.

Clinical Presentation

Classic Alport syndrome generally presents in childhood with hematuria, followed by proteinuria, hypertension, and progressive renal failure warranting a need for hemodialysis and eventually renal transplantation in the third decade of life. Ocular findings generally appear in adolescence and often coincide with the onset of high-tone sensorineural hearing loss and renal failure. Classic ocular findings include posterior polymorphous corneal dystrophy (less common), anterior lenticonus, and fleck retinopathy (e.g., dot-and-fleck retinopathy) found in the macula and midperipheral retina. Other ocular findings that have been described include juvenile arcus, microcornea, spherophakia, cataract (anterior polar due to lens capsule rupture), bulls-eye maculopathy, giant macular hole, temporal macular thinning (Ahmed et al. 2013), and vitelliform maculopathy (Fawzi et al. 2009). These ocular findings are similar in the XLD and AR forms of Alport, whereas typically only fleck retinopathy and cataract are found in the AD form. ERG and EOG are typically normal even in the presence of fleck retinopathy (Jeffrey et al. 1994). Subnormal ERGs have been reported in patients undergoing long-term dialysis, and it is unclear whether the subnormal ERG is due to renal disease, long-term hemodialysis, or the RPE basement membrane dysfunction from Alport syndrome. Reported VEP results are variable, ranging from normal to reduced amplitude and increased latency, with subnormal VEP generally found among those with renal dysfunction. The whitish-yellow flecks have been reported in both the superficial and deep layers of the retina. Histopathologic study of normal retina shows that the α3(IV), α4(IV), and α5(IV) collagen chains are present in both the ILM and the RPE basement membrane, even though the ILM is not a true basement membrane. Optical coherence tomography of flecks localizes to the ILM/RNFL layer, rather than the RPE/Bruchs membrane. Segmentation analysis in one study showed that there was thinning of both the ILM/RNFL and RPE basement membrane (Savige et al. 2010). The localization of the flecks to the superficial retinal layers and the often normal ERG and EOG have led some to postulate that perhaps the fleck retinopathy arises from dysfunction of the Mueller cells.

Diagnostics

Clinical suspicion for Alport syndrome should be confirmed with a tissue biopsy, either of the skin or kidney. Diagnosis is based on histologic evidence of abnormalities in the expression of

α3(IV), α4(IV), and α5(IV) collagen in the basement membrane of the epidermis of the skin or the glomerulus of the kidney. Demonstration of lamellation of the glomerulus basement membrane is also diagnostic. It has been recommended that genetic testing be reserved for prenatal screening, when biopsy of the skin or kidney is nondiagnostic or when mode of inheritance needs to be determined.

Differential Diagnosis

Other syndromes involving renal disease and retinopathy includes:

Type II membranoproliferative glomerulonephritis – the retinopathy found in this disease manifests as drusen-like deposits rather than flecks.

Alstrom disease – there is early, severe vision loss in this disease with fundus findings more similar to retinitis pigmentosa rather than fleck retinopathy.

Bardet-Biedl complex disorders – pigmentary retinopathy is found in this syndrome along with systemic manifestations of short stature, obesity, diabetes mellitus, developmental delay, polydactyly, and renal disease.

Senior-Loken syndrome – retinitis pigmentosa in conjunction with familial juvenile nephronophthisis.

Other syndromes involving deafness and retinopathy includes:

Usher syndrome – retinitis pigmentosa with sensorineural hearing loss.

Alstrom disease – pigmentary retinopathy with sensorineural hearing loss, renal insufficiency, short stature, dilated cardiomyopathy, and diabetes mellitus.

Cockayne syndrome – genetic defect in DNA repair leads to this syndrome consisting of pigmentary retinopathy, sensorineural hearing loss, short stature, premature aging, developmental delay, and microcephaly.

Refsum disease – hereditary neuro-cutaneous syndrome arising from defect in peroxisomal enzyme leading to phytanic acid accumulation. Signs include retinitis pigmentosa, anosmia, peripheral polyneuropathy, cerebellar ataxia, and ichthyosis.

Other fleck retinopathies that need to be distinguished from that found in Alport syndrome include Stargardt, fleck retinopathy of Tandoori, retinitis punctata albescens, fundus albipunctatus, and vitamin A deficiency.

Prophylaxis

Genetic counseling and examination of family members should be performed.

Therapy

Treatments for anterior lenticonus and cataract formation include correction of refractive error and lens replacement. The dot-fleck retinopathy is generally asymptomatic. Angiotensin-converting enzyme inhibitors and ARB are used to treat proteinuria and delay the onset of renal failure. Eventually, renal transplantation will be warranted.

Prognosis

Vision generally remains unaffected with dot-fleck retinopathy. Mortality arises from complications relating to kidney disease.

Epidemiology

The prevalence of Alport syndrome has been estimated at 1:50,000 live births. There is no gender predilection, but males are often more severely affected than females. The most common inheritance pattern is XLD (80%), followed by AR (15%) and then AD (5%). Ocular manifestations such as dot-and-fleck retinopathy occur in 85% males with XLAS, and anterior lenticonus occurs in 25% males with the XLAS

(Colville and Savige 1997). PPMD is a rare but well-described ocular finding.

Cross-References

- ▶ Alström Syndrome
- ▶ Bardet–Biedl Syndrome, Renal
- ▶ Fundus Albipunctatus
- ▶ Stargardt Disease
- ▶ Retinitis Punctata Albescens
- ▶ Vitamin A Deficiency

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Alström Syndrome

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Definition

Alström syndrome (AS) is a poorly understood, rare autosomal recessive syndrome that includes congenital retinal dystrophy leading to blindness, hearing impairment, metabolic syndrome, and other systemic manifestations.

Etiology

Alström syndrome is an autosomal recessive multisystem disorder due to mutations in the *ALMS1* gene. This gene is located on the short arm of chromosome 2 (2p13) and contains 23 exons. The protein is 4,169 amino acids in length and contains a large tandem-repeat domain that makes up about 40% of the entire protein (Hearn et al. 2002). It is ubiquitously expressed and appears to be necessary for function of ciliated cells. Mutations commonly occur in exons 8, 10, and 16, and different mutations appear to cause variable degrees of severity of disease.

Clinical Presentation

The ocular manifestations of AS include severely impaired vision, nystagmus, and photodysphoria by age 15 months. Unfortunately, ultimate vision will likely be at the light perception level by age 15 years. Anterior exam may demonstrate posterior subcapsular cataract. Examination of the fundus early on in the disease course typically reveals narrowing of the retinal vasculature. Later, optic nerve pallor and atrophy of the retinal pigment epithelium with increased visibility of choroidal vessels will be seen. The visual fields are generally constricted, and electrophysiologic testing will show progressive cone-rod dystrophy by early childhood (Russell-Eggitt et al. 1998; Malm et al. 2008). Optical coherence tomography of patients with AS demonstrates retinal immaturity and mild changes early, with progressive loss of retinal pigment epithelium and photoreceptors as the disease progresses (Vingolo et al. 2010).

Systemic manifestations of AS involve multiple organ systems (Russell-Eggitt et al. 1998; Marshall et al. 2005). Almost all individuals with AS will have metabolic syndrome – obesity, type II diabetes mellitus with hyperinsulinemia, and hypertriglyceridemia. Obesity is typically present by early childhood and may be exacerbated by the lack of physical activity due to vision and hearing loss. The insulin resistance may ultimately require insulin to control the hyperglycemia. Growth may be accelerated early, but

ultimate adult height will be below the 5th percentile. Affected individuals have wide, thick, and flat feet and short, stubby fingers but no poly/syndactyly as seen in Bardet-Biedl syndrome. Acanthosis nigricans can be present. Sensorineural hearing loss occurs frequently, often complicated by chronic otitis media. Developmental milestones may be delayed because of the sensory deficits that accompany this disease.

Individuals with AS commonly have dilated cardiomyopathy and congestive heart failure. This can occur abruptly during infancy, prior to the other symptoms of AS. These individuals typically survive and may have an interval of normal cardiac function, but then suddenly have a recurrence of heart failure in adolescence or adulthood. Others develop heart failure for the first time as adolescents or adults. Chronic bronchitis or frequent episodes of bronchopneumonia also occur. Hepatic dysfunction begins as silent elevation of liver enzymes and steatosis. This progresses to inflammatory infiltration, to fibrosis, and ultimately to cirrhosis. Hypogonadotropic hypogonadism can be present, with male patients demonstrating small external genitalia and testicular atrophy. Females with AS may present with pubertal delay and signs of hyperandrogenism. No individuals with AS are known to have reproduced. Patients with AS may also have urologic disturbances and progressive renal dysfunction. Renal failure is another common cause of mortality.

Diagnostics

Diagnosis can be made based on the clinical presentation. Diagnostic criteria vary according to age, but generally include poor vision with nystagmus or photophobia, abnormal electrophysiology, obesity, type II diabetes mellitus, and dilated cardiomyopathy or congestive heart failure. A family history may be present. Genetic testing by sequencing the *ALMS1* gene can be positive in up to 70% of cases.

Differential Diagnosis

In infants and children presenting with poor vision and associated nystagmus/photophobia, the differential diagnosis includes Bardet-Biedl syndrome (BBS), congential achromatopsia, Leber's congenital amaurosis (LCA), and Alport syndrome. The following features help distinguish AS from these conditions.

Bardet-Biedl Syndrome (*BBS*): Individuals with BBS have a similar clinical picture to AS, including vision loss, short stature, obesity, type II diabetes mellitus, and renal disease. Patients with BBS typically have mental retardation and poly/syndactyly, which are not features of AS. Their vision loss is generally not as severe as in AS. Moreover, dilated cardiomyopathy and sensorineural hearing loss are generally not features of BBS.

Congenital Achromatopsia/Rod Monochromatism: Congenital achromatopsia is a generally stationary retinal disorder with loss of cones but relatively normal rod function. Thus, visual acuity will be diminished but generally does not decrease past the 20/200 level. Clinical exam may show minimal retinal abnormalities. The electroretinogram will exhibit nearly absent cone response but nearly normal rod response. The systemic findings of AS such as obesity, metabolic syndrome, and cardiomyopathy are not characteristic of congenital achromatopsia.

Leber's Congenital Amaurosis: Leber's congenital amaurosis is a multigenic disease. The clinical exam in LCA is variable. Similar to AS, patients with LCA will have profound vision loss. They may also exhibit oculo-digital behavior. The electroretinogram will show extinguished photopic and scotopic response. Systemic features of AS are not characteristic of LCA.

Alport Syndrome: Alport syndrome is an oculo-auditory-renal syndrome comprised of glomerulonephritis, sensorineural hearing loss, and ocular findings. The ocular findings generally include posterior polymorphous corneal dystrophy and fleck retinopathy. Electroretinogram is generally normal. Alport syndrome does not have the systemic finding of metabolic syndrome, and the vision loss generally appears later than in Alström syndrome.

Prophylaxis

Genetic counseling and examination of family members should be performed.

Therapy

Ocular: Monitoring and supportive therapy, including low vision aids, is recommended.

Systemic: Management of systemic manifestations includes control of blood glucose and triglyceride levels. Individuals with AS should be monitored by appropriate subspecialists, including endocrinology, cardiology, gastroenterology, and nephrology. Genetic counseling for the patient and family members should be initiated.

Prognosis

Unfortunately, ocular prognosis is poor. Patients typically have progressive retinal degeneration with visual acuity decreasing to the light perception range by the teenage years. Mortality is frequently due to complications of cardiomyopathy and renal failure. Organ transplantation for end-stage disease of a single organ is hampered by the systemic nature of this disease.

Epidemiology

- No gender predilection.
- <1:100,000.
- Only about 300 cases have been reported.

Cross-References

- ▶ Alport Disease/Syndrome, Renal
- ▶ Bardet–Biedl Syndrome, Renal
- ▶ Congenital Anisocoria

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Alternating Light Test

▶ Swinging-Light Test, for RAPD Identification

Alternating Skew Deviation

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Synonyms

Hertwig-Magendie sign; Magendie-Hertwig sign; Skew deviation

Definition

Skew deviation is an acquired vertical strabismus with hypertropia (upward deviation of the eye) in one or both eyes. Skew deviation may be classified into three categories. Type 1 (utricle) skew deviation involves unequal (with different amplitudes) upward deviation of both eyes. Type 2 skew deviation (one eye is hypertropic and the fellow eye remains in primary position) is commonly seen in patients with Wallenberg syndrome, which involves infarction of the dorsolateral medulla oblongata. The excyclotropia of the ipsilateral eye is associated hypertropia of the contralateral eye. Type 3 skew deviation results from damage to the superior portion of the brainstem, such as the pons or medulla. Type 3 skew involves contralateral hypertropia in one eye and ipsilateral hypotropia (downward deviation of the eye) in the other eye.

Etiology

The causes of skew deviation include lesions to the brainstem or cerebellum or damage of the prenuclear vestibular input to the ocular motor nuclei. The most common events which result in skew deviation are brainstem or cerebellar stroke, demyelination, tumor, and head trauma.

Clinical Presentation

Patients with skew deviation typically complain of binocular vertical diplopia but may have other symptoms related to other posterior fossa signs.

Diagnostics

The diagnosis of skew deviation includes a complete eye exam to exclude alternative causes of the vertical deviation (e.g., extraocular muscle, myasthenia gravis). The vertical deviation in skew deviation typically does not localize to any one muscle or nerve innervation and due to otolith innervation. One method for differentiating isolated fourth nerve palsy from skew deviation is testing for torsion. In an ipsilateral fourth nerve palsy, ipsilateral excyclotorsion would be expected, but in skew, there might be bilateral torsion toward the hypotropic eye or other combinations of torsion that do not match for a fourth nerve palsy alone. Another method to potentially differentiate skew deviation from other causes of vertical strabismus is to perform an upright-supine test of the alignment. Patients who have skew deviation instead of another form of vertical strabismus (e.g., fourth nerve palsy) typically report and improvement of symptoms and reduction of the hypertropia when they change position from upright to supine position.

Differential Diagnosis

Other considerations in vertical strabismus include ocular motor cranial neuropathy, neuromuscular disorders, restrictive, and decompensated fusional disorders.

Therapy

Treatment should be directed at the underlying etiology. Patching, prism, or strabismus surgery can be offered as potential treatments.

Prognosis

Depends on the underlying etiology.

Epidemiology

Skew deviation may occur in individuals of any age or gender, but it is most commonly seen in older individuals with a history of vascular problems because ischemia is a common cause of skew deviation.

Cross-References

▶ Wallenberg Syndrome

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Altitudinal Visual Field Defects

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Synonyms

Superior or inferior altitudinal visual field defects

Definition

An altitudinal visual field defect is a condition in which there is defect in the superior or inferior portion of the visual field that respects the horizontal midline. The altitudinal defect can be unilateral or bilateral. The most common cause of this type of nerve fiber layer visual field defect in adults is glaucoma, but any process that damages the retinal nerve fiber layer can produce an altitudinal visual field defect including retinal vascular damage (e.g., branch retinal artery occlusion), nonarteritic and arteritic anterior ischemic optic neuropathy, optic disk drusen, papilledema, and other lesions producing optic nerve damage. Rarely juxtaposed homonymous quadrantanopic or hemianopic visual field defects can mimic bilateral altitudinal visual field loss. The optic nerve in altitudinal visual field loss may show sector or diffuse edema, be normal, or show optic atrophy. Disk drusen, glaucomatous cupping, optic atrophy, papilledema, or anterior optic neuropathies typically are clinically distinguishable by history or exam.

Cross-References

▶ Eyelid Trauma

Further Reding

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Amaurosis Fugax

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Synonyms

Transient monocular visual loss

Definition

Amaurosis fugax (from the Greek *amauros*, meaning dark or *obscure*, and *fugax*, meaning fleeting) is a subtype of transient monocular visual loss attributed to ischemia or vascular insufficiency. Typically, patients describe a painless, diminished, or absent vision in one eye that lasts few minutes, followed by complete recovery. Patients often depict the loss of vision as a shade or curtain that obscures vision in one eye; vision loss may be altitudinal, central, or peripheral (1990).

Most episodes of transient monocular visual loss last 2–20 min and then resolve spontaneously. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) found that the duration of the episodes ranged from 15 s to 23 h, with a median duration of 4 min (Ritter and Tyrrell 2013).

Rarely, patients with amaurosis fugax will complain of transient monocular blindness after exposure to bright light, these patients presenting an inability of borderline ocular circulation to sustain the increased retinal metabolic activity associated with exposure to bright light.

Etiology:

(a) Thromboembolic: some of the events are considered to be due to emboli reaching ophthalmic circulation from ipsilateral common carotid artery and its branches.
(b) Hemodynamic: occurring less frequently, when visual loss is precipitated by change in posture, exercise, or exposure to bright light, and it is most likely due to retinal vascular insufficiency.
(c) Idiopathic: some patients with monocular transient visual loss have no demonstrable ocular or systemic explanation for their symptoms; in some cases the mechanism may be vasospastic.

Diagnostic evaluation: ophthalmic examination, laboratory studies (complete blood count, sedimentation rate screening for hyperlipidemia diabetes, in younger patients search for thrombophilia), and duplex carotid for estimation of the degree of internal carotid stenosis. If the results of duplex are normal, computerized tomography or magnetic resonance imaging is recommended to provide evidence of clinically silent cerebral embolism. The risk of stroke in patients with amaurosis fugax is lower than that associated with hemispheric TIA (2% vs. 8%) (1991).

Treatment: if not contraindicated, antiplatelet therapy with aspirin 81–325 mg should be instituted in all patients with amaurosis fugax to reduce the risk of stroke; often, an aspirin-dipyridamole combination is prescribed, although the addition of dipyridamole is controversial.

Because the risk of stroke after amaurosis fugax is lower than that after hemispheric stroke, the guidelines for management of high-grade >70% internal carotid stenosis differ slightly between these two groups, tending to favor medical therapy for patients with isolated transient monocular visual loss. However, other factors have been used to stratify stroke risk in patients with amaurosis fugax, including male sex, age over 75 years or older, previous history of hemispheric stroke intermittent claudications, and stenosis of 80–94%. Patients with none or only one of these risk factors had a very low 3-year risk of ipsilateral stroke; for patients with three or more risk factors, the stroke risk is increasing to 24.2%. Surgical management – carotid endarterectomy – may have benefit for patients with amaurosis fugax who have three or more risk factors for stroke (Benavente et al. 2001).

Cross-References

- ▶ Monocular Transient, Visual Loss Embolic Causes of
- ▶ Monocular Transient Visual Loss, Hypoperfusion Causing
- ▶ Monocular Transient Visual Loss in Carotid Artery Disease
- ▶ Monocular Transient Visual Loss, Ocular Causes of
- ▶ Monocular Transient Visual Loss, Orbital Causes of
- ▶ Monocular Transient Visual Loss, Stroke After
- ▶ Monocular Transient Visual Loss, Systemic Causes of

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Amaurotic Familial Idiocy

► Tay-Sachs Disease (GM2 Gangliosidosis Type I)

AMD

► Age-Related Macular Degeneration

Ametropia: Definition

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Introduction

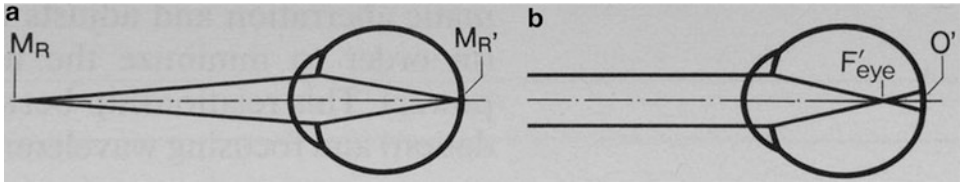
An eye is defined as ametropic if its far point does not lie at infinity. An (infinitely) far object point is then no longer imaged as a point on the retina. If the cornea and the crystalline lens have spherical surfaces, identical optical conditions are present in all meridian planes, and the eye is spherically ametropic.

If, however, the refracted rays only converge in two meridian planes (principal meridians) perpendicular to each other, the eye is termed astigmatically ametropic.

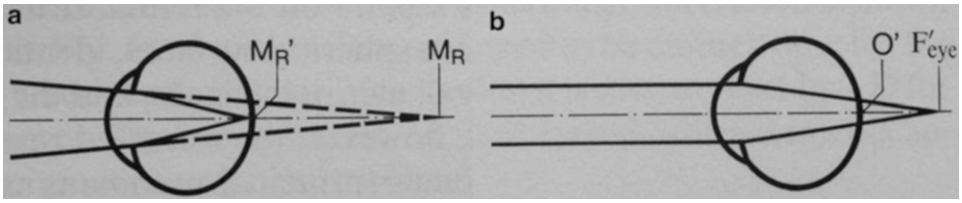
Kinds of Ametropia

Myopia: An eye is defined as myopic if its far point is located at a real finite distance in front of it. Far point refraction is negative: $K < 0$. The myopic eye usually has an overall length which is too long in comparison with the refractive power of the average emmetropic eye (axial myopia). Occasionally, it has a refractive power F_R which is too high in relation to the overall length of the standard eye (refractive myopia). The image-side focal point F'_{eye} of the eye with static accommodations lies inside the eye in front of the retina and an (infinitely) distant object is unsharply imaged in circles of confusion on the retina. As the near point of a myopic eye is also real in front of the eye, the accommodation range is real (Fig. 1).

Hypermetropia: An eye is termed hypermetropic if its far point is virtual behind it. Far point refraction is positive: $K > 0$. The overall length of the hypermetropic eye is usually too short in relation to the refractive power of the average emmetropic eye (axial hypermetropia). Occasionally the refractive power F_R is too low in relation to the overall length of the average emmetropic eye (refractive hypermetropia). The focal point F′eye of the eye with static



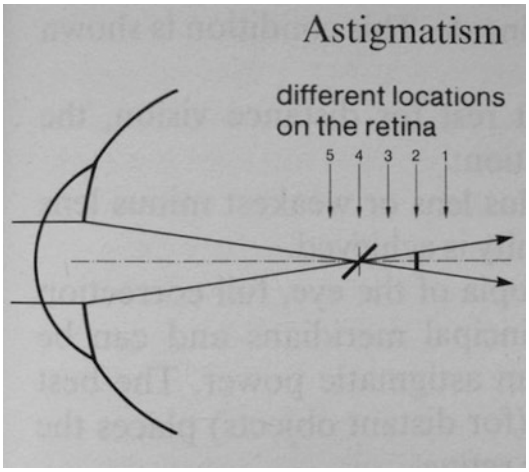
Ametropia: Definition, Fig. 1 Myopic eye (**a**) far point (**b**) focal point



Ametropia: Definition, Fig. 2 Hypermetropic eye (**a**) far point (**b**) focal point

accommodation lies behind the retina, and a (infinitely) distant object is unsharply imaged in circles of confusion on the retina. The location of the near point is dependent on the maximum amplitude of accommodation of the eye. If the latter is smaller than the far point refraction ($\Delta A_{max} < K$), the near point is virtual, and a virtual accommodation range also results. For $\Delta A_{max} = K$ the near point lies at infinity, and for $\Delta A_{max} > K$, the near point is real in front of the eye, with the result that part of the accommodation range is real. Appropriate accommodation increases the visual acuity of a hypermetropic eye, as the focal point then comes closer to the retina (Fig. 2).

Astigmatism: An astigmatically ametropic eye has two different far point locations for the two principal meridians with the refractive powers F_{RI} an F_{RII}. The (first) principal meridian with the higher refractive power F_{RI} is frequently almost vertical. This is astigmatism with the rule (astigmatismus rectus). If the principal meridian with the higher refractive power is almost horizontal, astigmatism against the rule (astigmatismus inversus) is present. In all other directions of the principal meridians, the astigmatism is called oblique astigmatism (astigmatismus obliquus). Each principal meridian itself can be emmetropic, myopic, or hypermetropic, with a line resulting as the image of an (infinitely) distant object. Further designation of the astigmatism is therefore dependent on the position of the two focal lines relative to the retina. Corneal and lenticular astigmatism exist (with corneal astigmatism occurring more frequently). Both together (but not by simple addition) give the total astigmatism. The difference between the total astigmatism and the corneal astigmatism is sometimes called the residual or physiological astigmatism (Fig. 3).



Ametropia: Definition, Fig. 3 Designation of the astigmatism. (*1*) Compound myopic astigmatism. (*2*) Simple myopic astigmatism (astigmatismus myopicus simplex). (*3*) Mixed astigmatism (astigmatismus mixtus). (*4*) Simple hypermetropic astigmatism (astigmatismus hyperopicus simplex). (*5*) Compound hypermetropic astigmatism (astigmatismus hyperopicus compositus)

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Amnion

▶ Transplantation, Amniotic Membrane

Amnion Graft

▶ Amniotic Membrane Transplantation Nonpharmacotherapy

Amnion Transplantation

▶ Amniotic Membrane Transplantation Nonpharmacotherapy

Amniotic Fluid Embolism, Purtscher-Like Retinopathy

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Synonyms

Purtscher's like retinopathy

Definition

Purtscher's retinopathy is an occlusive microvasculopathy which was first described in 1910 by Otmar Purtscher. The estimated incidence is 0.24 persons per million per year (Ashish and Martin 2006; Retina and Vitreous 2014–2015).

Etiology

Purtscher's retinopathy generally occurs as a result of cranial trauma or thoracic compression. When the etiology is nontraumatic, it is referred to as Purtscher-like retinopathy. Common causes of Purtscher-like retinopathy include acute pancreatitis, renal failure, amniotic fluid emboli, and autoimmune disease (Ashish and Martin 2006).

It is hypothesized to be caused by complement activation which causes granulocyte aggregation and leukoembolism. This process in turn occludes small arterioles such as those found in the peripapillary retina.

Clinical Presentation

Fundoscopic findings include Purtscher flecken (which consists of multiple areas of retinal whitening in the superficial aspect of the inner retina, between the arterioles and venules), cotton-wool spots, retinal hemorrhages (usually flame shaped), and optic disc edema, occasionally accompanied with afferent pupillary defect. The retinal whitening may extend to the edge of an adjacent venule but a clear zone usually exists between the affected retina and an adjacent arteriole. If the retinal whitening encircles the fovea, then a pseudo-cherry-red spot may be seen. These fundus abnormalities are usually confined to the posterior pole.

Without treatment, the above findings may resolve spontaneously within 1–3 months and maybe replaced by mottling of the retinal pigment epithelium, temporal disc pallor, and attenuation or sheathing of the retinal vessels (Ashish and Martin 2006; Retina and Vitreous 2014–2015).

Diagnosis

The diagnosis of these retinopathies is based on clinical findings and supported by fluorescein angiography. Patients usually present with sudden vision loss of variable severity in one or both eyes, hours up to days following the onset of the associated illness. Loss of vision may be accompanied by visual field loss such as central or paracentral scotoma. Peripheral visual function is usually preserved.

Fluorescein angiography (FA) findings include non-perfusion of the smaller retinal arterioles or capillaries, late leakage from the retinal vessels in areas of ischemia, and leakage from the optic nerve (Ashish and Martin 2006; Retina and Vitreous 2014–2015).

Differential Diagnosis

The differential diagnosis includes branch or central retinal artery occlusion, commotio retinae,

and fat embolism (Retina and Vitreous 2014–2015).

Therapy

There are no definite guidelines upon treatment for this condition. One should approach and treat the precipitating illness. Notable improvement of visual outcomes has been reported using high-dose intravenous steroids (Ashish and Martin 2006).

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Amniotic Membrane Graft

► Amniotic Membrane Transplantation Nonpharmacotherapy

Amniotic Membrane Transplantation Nonpharmacotherapy

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Synonyms

Amnion graft; Amnion transplantation; Amniotic membrane graft

Definition

Amniotic membrane transplantation (AMT) is the use of the innermost layer of the fetal amniotic sac as a graft in ocular surface surgery. The amniotic membrane (AM), also known as the amnion, is comprised of epithelium, basal lamina, and stromal matrix. It is avascular and does not trigger a clinically relevant immunologic response when transplanted. Amniotic membranes are obtained through elective cesarean section and preserved in either a dry or a wet form for later use.

Indication

Indications for the use of amniotic membrane transplantation can be divided into two categories: conjunctival surface reconstruction and corneal surface reconstruction. Defects in the conjunctival tissue most commonly arise from the surgical treatment of a variety of pathological processes, including ocular surface squamous neoplasia, pterygium, symblepharon release, and conjunctivochalasis. To repair these conjunctival defects, first the diseased conjunctiva is removed, and then AM is grafted to provide a suitable scaffold for epithelial proliferation and differentiation. AMT can be used similarly for defects in the cornea. Examples of pathologic conditions that result in corneal defects either directly or indirectly through the treatment of the condition are band keratopathy, bullous keratopathy, tumor excision, and non-healing stromal ulcers. When used to reconstruct the cornea, AM serves the same purpose as when used to reconstruct the conjunctiva, namely, providing a scaffold for corneal epithelium growth. AMT use is also indicated for corneal perforations due to trauma, acute chemical, and thermal burns, as well as for acute Steven-Johnson syndrome (SJS). Ocular surface damage can be quite extensive in cases of thermal/chemical burns and SJS, but as long as there is not a total limbal stem cell deficiency, AMT can prevent scarring, minimize symblepharon formation, and reduce limbal stromal infiltration.

Contraindication

Amniotic membrane transplantation serves as a substrate for limbal epithelial stem cell and

conjunctival epithelial stem cell growth to heal the defect. As the success of the transplant is reliant on the recipient's ability to provide epithelial and mesenchymal cells, amniotic membrane cannot be used in conditions where the limbal and conjunctival epithelial stem cells have been compromised or are absent. Amniotic membrane transplantation can therefore not be used in cases of severe aqueous tear deficiency, diffuse keratinization, absence of blinking in severe neurotropic state, or stromal ischemia.

Techniques and Principles

Amniotic membranes are obtained though elective cesarean section and preserved in either a dry or wet form. All prospective donors are screened for communicable diseases such as HIV, hepatitis, and syphilis. The tissue is cleaned in a mixture of antibiotics and cut into appropriate sizes; a single donor may provide sufficient tissue for 25–50 transplants. The amniotic membrane is then either cryopreserved or freeze dried to produce the wet and dry forms, respectively, which can be used for transplant.

The goal of amniotic membrane transplantation is to reconstruct the ocular surface, reduce inflammation, and promote epithelialization. Depending on the indication, the amniotic membrane can be used as either a patch or as a graft. When used as a patch, the amniotic membrane is temporarily placed over the defect on the surface of the eye and acts as a protective bandage. The patch is secured with the epithelial side up, and it acts as a barrier to the chemical constituents in the tear film. The patch also reduces inflammation through its anti-inflammatory properties. The patch is eventually removed or falls off. When used as a graft, the amniotic membrane is cut to match the defect and is fixed in place with the epithelial side up. This technique enables the amniotic membrane to act as a pseudo-basement membrane, which allows the recipients' own epithelial cells to migrate over the graft leading to faster healing. The graft becomes integrated with the host tissue and is therefore permanent.

Outcome

The outcomes of AMT differ depending on the underlying condition for which it is being used and the degree of inflammation. Most uses of AMT have demonstrated positive outcomes; however, outcomes from its use in conditions such as bullous keratopathy still remain controversial.

Complications

The most serious complications associated with amniotic membrane transplantation are failure to obtain the desired results or recurrence of the original defect requiring subsequent transplantation. The membrane may also become loose and fall out, although this can be avoided by suturing it in place or using a bandage contact lens. AMT may result in corneal calcification, which can impair vision. It is also possible that the subepithelial layer of the membrane persists, resulting in some opacification of the visual fields. Complications associated with the surgery itself include infection, suture granuloma, hematoma, and sterile hypopyon.

Cross-References

- ▶ Calcific Band Keratopathy
- ▶ Chemical Injury (Burns)
- ▶ Conjunctiva
- ▶ Conjunctivochalasis
- ▶ Corneal Ulcers
- ▶ Corneoscleral Laceration
- ▶ Deep Anterior Lamellar Keratoplasty (DALK)
- ▶ Keratitis
- ▶ Keratoconjunctivitis: Overview
- ▶ Limbal Stem Cells
- ▶ Pemphigoid, Cicatricial
- ▶ Primary Endothelial Failure, After Penetrating Keratoplasty
- ▶ Pterygium
- ▶ Stevens Johnson Syndrome
- ▶ Symblepharon

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Amorphous Corneal Dystrophy, Posterior Disease

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Synonyms

Posterior amorphous corneal dystrophy

Definition

Posterior amorphous corneal dystrophy (PACD) is a rare, hereditary condition of the posterior stroma resulting in sheetlike opacity, corneal flattening, and thinning of the cornea.

Etiology

PACD has been identified in several families worldwide with a hereditary distribution consistent with autosomal dominant inheritance. Linkage and haplotype analyses have identified a locus at 12q21.33 in a single family with PACD; mutations in candidate genes KERA, LUM, DCN, and EPYC at this locus have been ruled out. Posterior stromal opacity is secondary to disorganization of stromal fibrils; histological studies have shown no evidence of deposition with hematoxylin-eosin, Masson trichrome, or Alcian blue stains. Electron microscopy has shown amorphous extracellular material between stromal lamellae in the anterior cornea, although its visual significance is unclear.

Clinical Presentation

Patients present with bilateral, symmetric corneal opacification affecting the posterior cornea at the level of or slightly anterior to Descemet's membrane. These focal opacities are gray-white and sheetlike in appearance. Areas of clear cornea are interspersed between opacities, which are present paracentrally or peripherally; visual acuity is therefore generally well maintained. Corneal thickness was approximately 453 μm and average corneal curvature 39.1 diopters in the largest series of 20 affected individuals in a single pedigree. Iris abnormalities are variably present and include corectopia, coloboma, iridocorneal adhesions, and iris atrophy. Endothelium is inconsistently affected, ranging from focal attenuation to normal configuration. Secondary glaucoma may occur.

Diagnosis

The diagnosis of PACD is made clinically with slit-lamp biomicroscopy and can be confirmed with an autosomal dominant pattern of inheritance. Histological examination of corneal buttons submitted during penetrating keratoplasty may be used to confirm clinical findings. No genetic testing is yet available for diagnostic purposes.

Differential Diagnosis

Posterior polymorphous corneal dystrophy (PPCD) is also a posterior corneal dystrophy that can result in epithelialization of the corneal endothelium.

Prophylaxis

There is no known method of prophylaxis at this time.

Therapy

Patients with advanced disease limiting visual acuity may benefit from corneal transplantation. The choice of deep anterior lamellar keratoplasty or penetrating keratoplasty varies based on the distribution of opacities through the stroma and the extent to which Descemet's membrane is affected. Therapy must also be directed toward secondary features such as maintenance of adequate intraocular pressure and correction of refractive error.

Prognosis

Corneal endothelium typically remains intact centrally and patients maintain good vision.

Epidemiology

Rare; prevalence is unknown. PACD has been reported in several families throughout the world, mostly in North America and Europe.

Cross-References

▶ Fuchs' Corneal Dystrophy
▶ Posterior Polymorphous Corneal Dystrophy

Further Reading

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Amphotericin B

▶ Amphotericin B, for *Aspergillus* Endophthalmitis

Amphotericin B Colloidal Dispersion (ABCD)

▶ Amphotericin B, for *Aspergillus* Endophthalmitis

Amphotericin B Lipid Complex (ABLC)

▶ Amphotericin B, for *Aspergillus* Endophthalmitis

Amphotericin B, for *Aspergillus* Endophthalmitis

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Synonyms

Amphotericin B; Amphotericin B Colloidal Dispersion (ABCD); Amphotericin B Lipid Complex

(ABLC); Deoxycholate Amphotericin (D-AmB); Liposomal Amphotericin B (L-AmB)

Definition

Amphotericin B (AmB) is a heptaene polyene antifungal originally discovered as a metabolite of *Streptomyces nodosus*. AmB is a poorly water-soluble compound and has been combined with deoxycholate or placed in liposomes to improve its bioavailability.

AmB is effective against most *Aspergillus* species including *A. fumigatus*, *A. flavus*, and *A. niger*, while *A. Terreus*, *A. nidulans*, *A. ustus*, and *A. glaucus* can show resistance to AmB. This antifungal medication acts by binding to ergosterol, a sterol component of the cell membrane of susceptible fungi. This leads to the formation of transmembrane channels and subsequent ion leakage. Another possible mechanism of action of AmB is through lipoperoxidation of the cell membrane resulting in oxidative damage to the cell.

AmB binds to plasma protein and distributes into the reticuloendothelial tissues and the kidney. Following intravenous infusion of 1 mg/kg of D-AmB, a peak plasma concentration of 2–4 μg/mL is achieved with a half-life of 24–48 h. The recommended dosing regimen of D-AmB associated with minimum risk of systemic toxicity is 0.25–1 mg/kg/day given through a slow intravenous infusion over 2–6 h. In cases of invasive aspergillosis, a salvage therapy is recommended using lipid formulation of AmB. The recommended dose for ABLC and ABCD is 5 mg/kg/day and 3–4 mg/kg/day, respectively, while L-AMB is approved at a dosage of 3–5 mg/kg/day. In animal experiments with endotoxin-induced uveitis, systemic administration of AmB provides intraocular concentrations ranging from 0.47 μg/mL for D-AmB to 0.16 μg/mL for the lipid formulation of AmB.

Due to the low concentration of intraocular AmB obtained following systemic administration, intravitreal injections of (non-liposomal) AmB at doses of 5–10 μg with or without vitrectomy are the treatment of choice in fungal endophthalmitis with vitreous involvement. Intravitreal AmB is used as adjunctive therapy along with systemic antifungal agents in patients who have sight-threatening endophthalmitis caused by *Aspergillus* species. Following intravitreal administration, the half-life of AmB is 7–14 days, reduced to two days in vitrectomized eyes.

Adverse reactions against AmB include infusion-related reactions such as fever, rigors, chills, myalgias, arthralgias, nausea, vomiting, headaches, and bronchospasm. The therapeutic doses of AmB for aspergillosis can induce hepatotoxicity and nephrotoxicity; the latter occurs especially in the presence of concomitant nephrotoxic agents such as cyclosporine and tacrolimus. The risk of renal failure secondary to AmB is also more common in patients with background renal impairment and also patients suffering from diabetes mellitus.

Intravitreal injection of AmB at doses higher than the recommended dose has been reported to cause retinal toxicity, retinal detachment, and cataract although retinal toxicity has been documented even with intravitreal injections of 1 μg.

Even now, most of the information regarding the effectiveness and treatment outcome of AmB in *Aspergillus* endophthalmitis comes from case reports and series. Favorable response to intravitreal injection of AmB has been observed in some case reports of patients with *Aspergillus* endophthalmitis. However, poor visual outcome can still occur despite repeated intravitreal AmB injection combined with vitrectomy.

Cross-References

- ▶ Aspergillosis in Orbit
- ▶ Endophthalmitis
- ▶ Intraocular Injection of Ocular Drugs

Amyloidosis V

► Meretoja Syndrome

Amyloidosis V and Familial Amyloid Polyneuropathy Type IV (FAP-IV)

► Stromal Dystrophies

Amyloidosis/Amyloid Deposits, Vitreous Involvement in

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Definition

Amyloidosis encompasses a spectrum of disorders characterized by the abnormal deposition of insoluble protein aggregates. Amyloidosis can affect any organ and may be a localized or systemic disease. Ocular amyloidosis includes the orbit, extraocular muscles, conjunctiva, cornea, iris, trabecular meshwork, lens, vitreous, retina, and choroid. Ocular amyloidosis is a rare cause of vitreous haze and should be included in the differential diagnosis of vitreous opacification. The incidence of vitreous opacities in amyloidosis varies from 5.4% to 35%.

Vitreous amyloidosis manifests as "lacy," "cobweb-like," "sheet-like," or "stringy" veils of gray or yellowish-white material in the vitreous. It is frequently visually significant. Most cases show an initial retinal tuft adjacent to retinal vessels followed by secondary vitreous involvement. Bilateral disease is typical, but unilateral or highly asymmetric presentations exist. Symptoms include floaters, blurry vision, or glare, although patients may be asymptomatic. Displacement of a vitreous veil into the visual axis may manifest an acute decrease in visual acuity. Vitreous amyloidosis frequently arises in the setting of neuropathic heredofamilial systemic disease and is often accompanied by multiple organ involvement. Mutations in transport protein transthyretin (TTR), also known as prealbumin, are responsible for the majority of cases. Amyloidosis involving the vitreous has rarely been observed in nonfamilial cases. Differential diagnosis includes asteroid hyalosis and chronic (dehemoglobinized) vitreous hemorrhage. Diagnosis is made by a diagnostic vitrectomy with vitreous biopsy. The gold standard is Congo red staining which demonstrates apple-green birefringence when viewed through crossed polarimetric filters. In patients with visually significant vitreous amyloidosis, vitrectomy has been used with satisfactory results. Recurrence is common in the presence of systemic disease. Glaucoma may develop concurrently with vitreous amyloidosis or follow an independent time course. Filtering surgery may be indicated at the time of vitrectomy or at any time postoperatively. Direct seeding of the trabecular meshwork during surgery has been theorized as a possible mechanism for elevation in intraocular pressure. Based on the theory that the retinal pigment epithelium (RPE) is responsible for production of amyloidogenic transthyretin, panretinal photocoagulation (PRP) is being investigated as a possible therapy for recurrence of vitreous amyloidosis deposits. Most cases of vitreous amyloidosis are part of systemic amyloidosis. A therapy for systemic amyloidosis is needed. The treatment is typically managed by a rheumatologist. Conventional treatment includes prednisone and melphalan. Other agents include dexamethasone, thalidomide, etanercept, glycosaminoglycan analogues, and various types of targeted immunotherapy.

Analgesic Rebound Headache

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Synonyms

Drug-induced headache; Medication misuse headache; Medication overuse headache; Rebound headache

Definition

Analgesic rebound headache may be caused by any medications used to treat headache including triptans, ergotamines, opioids, and other analgesics. Analgesic rebound headache typically results from the chronic overuse of analgesics for headache relief and is defined as a headache that has started or has worsened from the use of analgesic medications. This condition is primarily seen in individuals who have a chronic headache disorder, such as migraine, and take analgesics for pain relief more than two to three times per week for a period of more than 3 consecutive months. Analgesic rebound headache may even interfere with the proper treatment of an underlying chronic headache disorder.

Etiology

The exact mechanism for analgesic rebound headaches is not understood. There are a number of factors that may contribute, including sensitization to the medication, genetics, biological influences, and psychological factors. It is important to note that while the overuse of analgesics to reduce headache can cause analgesic rebound headache, the overuse of analgesics for other causes has not been shown to cause headache. Further study is needed to clarify the exact mechanism and identify the specific drug components that trigger this condition. It is often difficult to determine which medications are strictly causative because patients are usually taking more than one medication at a time.

Clinical Presentation

The classic presentation of this disease is a patient who complains of chronic headaches and daily analgesic use. Often, the headaches may seem either caused by or exacerbated by the use of analgesics.

Diagnostics

The diagnosis of analgesic rebound headache is made on a clinical basis and no laboratory examination is necessary. It is important to rule out any organic alternative causes of primary and secondary headache prior to making the diagnosis of analgesic rebound headache.

Differential Diagnosis

When formulating a differential for these patients, one should consider any cause of primary or

secondary chronic headache. Among the primary causes of headache to rule out are chronic tension headache, chronic migraine headache, hemicrania continua, and new daily persistent headache. Some of the secondary causes of chronic headache to rule out include thrombosis of the venous sinuses and giant cell arteritis.

Prophylaxis

Any individual who has a chronic headache condition should be assumed to be at risk for developing analgesic rebound headache. In order to prevent this condition from occurring, medication should be aimed at controlling their underlying disease. Anticonvulsants, antidepressants, antihypertensives, and antihistamines may all be considered. In addition, there are some general strategies that may be employed. A headache diary may be kept in order to identify and avoid any headache triggering factors. Individuals should refrain from taking analgesics more than two times a week, follow a structured sleeping schedule, avoid skipping meals, become physically active, reduce stress, and quit smoking.

Therapy

The first step in the approach of the patient with analgesic rebound headaches is to quickly stop the medication that is suspected to have been overused. Upon stopping the offending medication, withdrawal symptoms may occur. These can last for up to 10 days and may include anxiety, headache, nausea, vomiting, tachycardia, hypotension, and changes in sleep patterns. It is important to educate patients who have rebound headaches that the overuse of medication is what is triggering their headaches and to encourage them to minimize the analgesic medication they have been using to less than 2 days per week or avoid it altogether. A prophylactic medication may be used for patients who have underlying causes of chronic headache, such as migraine, to prevent a flare-up of headaches following withdrawal from analgesics. After the patient has been instructed to discontinue usage of the offending medication, it is critical to follow up with them in order to see if they have actually been compliant and if there have been any new headache occurrences.

Prognosis

Withdrawal therapy has been shown to reduce headache days by 50% and success rates between 60% and 70% have been reported. Patients have the highest risk of relapse during the first year of withdrawal therapy. The risk of relapse has been determined to be dependent upon two main factors: the etiology of the primary headache and the type of medication that was overused. Patients with primarily tension-type headaches have a higher risk of relapse than patients with chronic migraine headache, and patients who overuse analgesics have a higher risk of relapse than those who overuse other medications. Factors such as the duration of analgesic overuse, the duration of analgesic rebound headache, and the use of prophylactic treatment were not shown to have a significant impact on relapse rate.

Epidemiology

Analgesic rebound headache is a growing problem because there is an increasing amount of people that overuse analgesic medications. Studies show that up to 4% of the population engages in analgesic overuse, and between 2% and 5% of the population have chronic headache. Analgesic rebound headache has a prevalence of 1% in the total population and is seen more commonly in women than in men. General risk factors for developing analgesic rebound headache include migraine headache, chronic tension-type headache, chronic headache, and low socioeconomic status. Of the different types of chronic headache associated with analgesic rebound headache, migraine is the most frequent one.

Cross-References

- ▶ Retinal/Ocular Migraine
- ▶ Rebound Headache

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Anatomic Reattachment Surgery, for Retinal Detachment

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Definition

It is a surgical procedure to reattach separated neurosensory retina back to the retinal pigment epithelium anatomically. The aim is to close each retinal break. For permanent closure of the breaks, elimination of vitreoretinal traction is mostly necessary.

Indications

Rhegmatogenous retinal detachment, tractional retinal detachment.

Pneumatic retinopexy: Retinal detachment with superior retinal break(s) extending less than 3 clock hours of retina

Scleral buckling: Rhegmatogenous retinal detachment, retinal detachment due to dialysis

Pars plana vitrectomy: Tractional retinal detachment, detachments with significant vitreous opacities, grade C–D proliferative vitreoretinopathy (PVR), macular hole retinal detachment, detachments due to giant retinal tears with PVR, thin sclera

Contraindications

Pneumatic retinopexy: Break(s) in the inferior 4-clock-hours, grade C or D PVR, lattice degeneration, uncontrolled glaucoma, uncooperative patient for head positioning, media opacities preventing complete peripheral retinal assessment

Scleral buckling: Grade D PVR, significant vitreous opacity preventing complete examination of the peripheral retina, sickle cell anemia, significantly posterior breaks, extremely thin sclera

Pars plana vitrectomy: Relatively simple phakic retinal detachment, inferior retinal dialysis

Techniques and Principles

Principles of reattachment surgery for retinal detachment are closure of the break(s), relief of traction, alteration of fluid currents and retinopexy (Williamson 2008). To attain these goals, various techniques can be applied:

Pneumatic retinopexy: Minimally invasive technique involving injection of gas (0.4–0.6 ml sulfur hexafluoride, SF_6, or 0.3–0.4 ml perfluoropropane, C_3F_8) into the vitreous cavity, retinopexy with cryotherapy at the same session, or laser photocoagulation 1–2 days later and head positioning to enable the gas bubble to oppose the break(s). A limbal paracentesis is generally performed before the injection of gas. If there is bullous retinal detachment near an attached macula, to prevent iatrogenic macular detachment, steamroller maneuver of gas is recommended before cryotherapy.

Scleral buckling: Traditionally the gold standard treatment for uncomplicated rhegmatogenous retinal detachment. The purpose is to indent the sclera toward the retina beneath the retinal break to limit the rate of fluid flow to the subretinal space and close the break(s) and to relieve vitreoretinal traction. To seal the break(s), cryotherapy or laser photocoagulation is employed.

The technique involves local or general anesthesia. Depending on the size of the planned buckle, after partial or complete circumferential limbal peritomy, two to four rectus muscles are slung with traction sutures, and sclera is examined for ectatic areas. Whole peripheral retina is examined with indentation and retinal breaks are marked on the sclera. Subretinal fluid may be drained at this stage. Cryotherapy or transscleral diode laser is applied around the edges of the break(s). Appropriate explant and if necessary encircling band are placed and sutured to the sclera. If necessary, air or gas is injected for internal tamponade. Ends of the encircling band are fastened to each other with a Watzke sleeve. Optic nerve head perfusion and position of the buckle are checked, traction sutures are removed, and the peritomy is closed (Sullivan 2013).

Materials that have been used for scleral buckling include fascia lata, human donor sclera, gelatin, hydrogel implants, silicone sponges, solid silicone tires, and bands. The last three are the most preferred materials currently. Selection of the scleral buckling element depends on number, location, orientation, and size of the break(s) and presence of vitreoretinal degeneration. Guidelines for selection can be summarized as follows (Rizzo et al. 2012):

Radial segmental buckling: A single retinal break, an atrophic hole, a flap tear, a large horseshoe tear, two breaks at different quadrants, posterior breaks with or without lattice degeneration

Circumferential segmental buckling: Multiple adjacent retinal breaks, retinal breaks with limited lattice degeneration, anterior retinal breaks, or retinal dialysis

Encircling buckling: Multiple retinal breaks at multiple quadrants, multiple retinal breaks with extensive lattice degeneration, absence of recognized breaks, total chronic detachment with fibrosis

Many surgeons supplement the segmental buckle, either radial or circumferential, with an encircling band.

Pars plana vitrectomy: First reserved for complex retinal detachments with vitreous pathologies, however with developments in sutureless small gauge and wide-field imaging techniques recently became the preferred method even for simple detachments

Standard technique involves creation of three ports through the pars plana, insertion of infusion cannula, core vitrectomy, detachment of posterior vitreous if not already present, peripheral vitrectomy with low suction and higher cutting speed, injection of perfluorocarbon liquid if the detachment is bullous, identifying each break with indentation, internal drainage of subretinal fluid from the original break via fluid-air exchange, retinopexy with endolaser or cryotherapy, air-gas exchange, and closure of the ports. In complex cases silicone oil may be used as the tamponade. Some surgeons add encircling buckle in the presence of widespread peripheral pathology.

Selection of a specific reattachment procedure depends on the type and location of retinal breaks, amount of vitreoretinal traction, and the lens status. All procedures can be used alone, consecutively or in combination.

Outcome

Primary success rate for pneumatic retinopexy was reported to be 74.4%, which increased to 96.1 with further operations (Chan et al. 2008). Ideal case selection and complete peripheral retinopexy for 360° increase the success rate to 97%. Scleral buckling is successful in 74–91% of the cases after a single operation. With further surgeries the ratio increases to 95%. With vitrectomy primary anatomic success is reported to be 74–92.9%. With additional surgeries this ratio increases to nearly 100%. In the scleral buckling versus primary vitrectomy study involving 681 patients, primary reattachment in phakic patients was similar, 73.7% with scleral buckling and 74.9% with vitrectomy, but in aphakic/pseudophakic patients vitrectomy was superior: 60.1% primary reattachment with scleral buckling and 79.5% with vitrectomy (Heimann et al. 2007). Best corrected visual acuity improvement was significantly marked in phakic cases with scleral buckling.

Causes of failure with these procedures are due to missed breaks, new breaks, reopening of a retinal break, inadequate buckle, misplaced buckle, fishmouthing, and most importantly PVR.

Complications

- Scleral rupture/perforation
- Rectus muscle rupture
- Damage to the vortex veins
- Intraocular hemorrhage
- Retinal incarceration
- Retinal perforation
- Iatrogenic retinal breaks
- Subretinal gas
- Fish egging of air or gas
- Trapped air or gas
- Fishmouthing
- Increased intraocular pressure
- Central retinal artery occlusion
- Lid swelling and/or chemosis postoperatively
- Ptosis
- Persistent retinal detachment/recurrence
- Symblepharon
- Anterior segment ischemia/necrosis
- Ciliochoroidal detachment (pre-, intra-, postoperatively)
- Persistent subretinal fluid
- Muscular imbalance/diplopia
- Cystoid macular edema
- Macular hole
- Changes in the refractive error
- Extrusion/infection of buckling material
- Band migration
- Endophthalmitis
- Epiretinal membrane
- Cataract
- PVR
- Phthisis bulbi

Cross-References

- ▶ Encircling Buckle
- ▶ Pars Plana Vitrectomy
- ▶ Retinal Detachment Rhegmatogenous
- ▶ Tractional Retinal Detachment

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Anatomically Narrow Drainage Angle

▶ Angle-Closure Suspect

Anecortave

▶ Anecortave Acetate (RETAANE), for Age-Related Macular Degeneration

Anecortave Acetate (RETAANE), for Age-Related Macular Degeneration

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Synonyms

15 mg anecortave acetate depot suspension; Anecortave; Retaane

Definition

Anecortave acetate (Retaane, Alcon, Inc.) is an angiostatic cortisone derived from cortisol which has been chemically modified to eliminate all glucocorticoid activity, thereby reducing ocular side effects such as glaucoma and cataracts (Tombran-Tink and Banrstable 2006). Due to lack of efficacy in a phase III clinical study of *age-related macular degeneration (AMD)*, it is no longer manufactured (Albert et al. 2008).

Indication

Although there are currently no official indications for anecortave acetate, it has been used successfully to treat *choroidal neovascularization* (CNV) secondary to AMD and primary open angle glaucoma. In addition, it has been studied as a potential prophylaxis for the progress of dry AMD to wet AMD (Roy et al. 2007).

Contraindication

There are no reported contraindications for anecortave acetate.

Use and Dosage

Though no longer available, anecortave acetate was originally manufactured as a 15 mg (0.5 ml of 30 mg/ml) and 30 mg dose (0.5 ml of 60 mg/ml). It is administered as a single posterior juxtascleral injections at 6 month intervals.

Adverse Reactions

Most adverse reactions associated with anecortave acetate result from the procedure itself. Reported ocular adverse events are cataract, decreased visual acuity, ptosis, eye pain, visual abnormalities, and *subconjunctival hemorrhage*.

Interactions

There are no reported interactions for anecortave acetate.

Cross-References

- ▶ Age-Related Macular Degeneration
- ▶ Choroidal Neovascularization
- ▶ Subconjunctival Hemorrhage

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Anesthesia (Anesthetics), Local

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Synonyms

Regional anesthesia

Definition

Local anesthesia for ophthalmic procedures refers to the administration of anesthetic agents either topically, intraocularly, or by injection.

Indication

Anesthesia for ophthalmic procedures is indicated to provide analgesia (pain relief) with or without

akinesia (elimination of extraocular motility). The route of administration depends on several factors, including surgeon and patient preference, patient's ability to follow commands, type and length of procedure, and amount of akinesia desired.

Topical anesthesia provides anesthesia of the conjunctiva, cornea, and anterior sclera. Topical anesthesia does not provide any akinesia. Topical anesthesia can be used for short duration procedures such as cataract surgeries. Advantages of topical anesthesia include quick visual recovery, avoidance of injection anesthesia, and lack of need to hold anticoagulation or antiplatelet therapy. Disadvantages may include patient discomfort with intraocular manipulation or pressure fluctuations and eye movements during surgery.

Intraocular anesthesia may be used as an adjunct to topical anesthesia during cataract surgeries, as it provides anesthesia for the intraocular structures such as the iris, as well as reduces the sensation of pressure fluctuations in the anterior chamber.

Injection anesthesia can be delivered by parabulbar, peribulbar, or retrobulbar routes and provides anesthesia to the ocular surface and intraocular structures. Injection anesthesia also allows for a decrease or elimination of the extraocular movements and thus is suitable for patients who are not able to follow commands, for surgeries that require extensive intraocular manipulation, or for lengthy procedures. Injection anesthesia requires that placement of a patch on the eye in the immediate postoperative period. Patients on anticoagulation or antiplatelet therapy may need there therapy discontinued to decrease the risk of a retrobulbar hemorrhage. Parabulbar injections are placed using a subtenon's incision, while peribulbar injections are generally delivered through the skin and orbicularis muscle. Retrobulbar anesthesia consists of placing the anesthetic agent more posterior than a peribulbar injection, into the intraconal region. A properly placed retrobulbar injection provides the most amount of akinesia.

Contraindication

Anesthetic agents are contraindicated in patients with known hypersensitivity to those agents. Contraindications to topical and injection anesthesia also include a perforating or penetrating globe injury.

Use and Dosage

Topical anesthesia can be achieved using solution or gel formulations of anesthetic agents, such as tetracaine, proparacaine, or lidocaine, directly on the surface of the eye. Topical agents include tetracaine (0.5%) and proparacaine (0.5%) drops or lidocaine gel (2%) or Akten TM 3.5% lidocaine gel. Agents used for injection anesthesia, such as lidocaine (1–4%), may also be used topically.

Intraocular anesthesia can be administered by injecting 0.1–0.5 ml of preservative free lidocaine (1%) into the anterior chamber using a paracentesis port.

Injection anesthesia can be administered using lidocaine (1% or 2%) with or without bupivacaine (0.75%). A total volume of 3–5 ml is generally used. Hyaluronidase can be used in conjunction with either of these two agents to facilitate the diffusion of the anesthetic agents through the orbital tissues.

Adverse Reactions

General:

Allergy to anesthetic agent

Topical anesthesia:

Superficial punctate keratopathy

Intraocular anesthesia:
Corneal edema (when anesthetic agents with preservatives are injected intraocularly)
Injection anesthesia:

Retrobulbar hemorrhage
Scleral perforation

Optic nerve or extraocular muscle damage
Oculocardiac reflex
Intravascular injection with CNS affects
Brain stem anesthesia

Interactions

Although drug interactions have been reported with local anesthetics, given the route of administration for ophthalmic cases and the small doses used, the incidence is rare. Adverse reactions are as noted above.

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Anesthesia, Cataract

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Synonyms

Cryoanalgesia; No-anesthesia cataract surgery

Definition

Cataract surgery without the use of anesthetics

Indication

Reserved to very experienced surgeons and moderate cataract in patients with good compliance and contraindication for topical anesthesia.

Contraindication

Mature cataract, expected complications during cataract surgery

Techniques and Principles

A few authors have described this technique. No-anesthesia cataract surgery can only be performed in selected patients (Shah 2010). During surgery, grasping the conjunctiva or sclera with toothed forceps should be avoided. By using clear-cornea incision, there is no need for cautery. Microscope luminance and the power used for phacoemulsification has to be kept as low as possible to avoid heating of the phaco tip.

Although not fully understood, this technique seems to be possible due to anatomic variations of corneal sensitivity: (Nouvellon et al. 2010) in the upper peripheral cornea, there is less density of inervational network and there are more free nerve endings in the horizontal than in the vertical one. As corneal sensitivity is declining by the age, this technique seems to work better in patients >60 years. In addition, there is a number of factors that have influenced on corneal sensitivity such as UV radiation, race, and corneal thickness.

Other no-anesthetic cataract surgery techniques use additionally chilled agents such as cooled eye pads or chilled viscoelastic material.

Outcome

According to a prospective study of Agarwal and colleagues, patients' pain is not differing form topical anesthesia (Pandey et al. 2001). However this study also showed that even though pain score was comparable in both groups the patient's as well as the surgeon's discomfort was higher in the no-anesthesia group of patients.

Complications

There is no study on specific complications using this technique. However, it seems clear that in

case of complications management thereof is difficult.

Cross-References

- ▶ Cataract Surgery
- ▶ Subtenon's Anesthesia
- ▶ Topical Anesthesia

References

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Aneurysm Retinal Arterial

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Definition

Retinal arterial macroaneurysm (RAM) is an acquired saccular or fusiform dilation of the arterioles of the retina. RAM typically develops within the first three orders of arteriolar bifurcations, especially at the site of an arteriolar bifurcation or at an arteriovenous crossing. The most commonly reported site for RAM is the superotemporal quadrant with involvement of the superotemporal artery, but also the nasal arteries can be affected, and less commonly the cilioretinal arteries or the optic nerve head vessels can even be involved.

Etiology

RAM is strongly associated with systemic hypertension and atherosclerosis. However, the exact pathophysiological mechanisms leading to the RAM development is not understood yet (Abdel-Khalek and Richardson 1986; Rabb et al. 1988; Brown et al. 1994). The most common hypothesis suggests that arteriosclerosis could lead to progressive fibrotic degeneration of the vessel wall. The consequent decrease in wall elasticity in combination with the elevated luminal pressure could result in the development of an arterial aneurysmal dilation. An alternative hypothesis is that emboli or even intra-arterial thrombosis could determine mechanical damages of the endothelium or the adventitial which predisposes the vessel to aneurysm formation.

Clinical Presentation

The diagnosis of RAM can be occasionally made on routine examination in cases of asymptomatic RAM, but can also be related to the occurrence of a sudden and painless loss of vision. The clinical picture may vary according to the stage of the disease. Classical appearance of RAM is characterized by the detection of a round-oval dilation along the course of a major retinal arteriole. RAM can be asymptomatic, without exudative manifestations, or can also be associated with extensive preretinal, intraretinal, subretinal, and sub-internal limiting membrane hemorrhages (Abdel-Khalek and Richardson 1986; Rabb et al. 1988; Brown et al. 1994). Moreover, other exudative manifestations can be visible, including neurosensory detachment, intraretinal cysts, and hard lipid exudates in a circinate pattern (Battaglia Parodi et al. 2011). The identification of macular intraretinal fluid can originate from RAM apparently located far away from the fovea, and the detection of fluid turns out to be easier using optical coherence tomography techniques. Pulsations of the aneurysm can be appreciated in 10% of cases (Rabb et al. 1988).

Natural History

The clinical aspect of RAM may remain unchanged for many years, but in the long run,

RAM eventually undergoes toward a progressive fibrotic involution. Thus, natural history may vary from the spontaneous obliteration of the lesion to a number of vision threatening complications, including subretinal, preretinal, or vitreous hemorrhages, macular edema, serous macular detachment, macular deposition of hard exudates, epiretinal membrane, macular hole, and branch retinal vein occlusion.

Diagnostics

In many cases, the simple biomicroscopic examination allows the direct identification of RAM. Ophthalmoscopy can clearly reveal a focal saccular or fusiform dilation of the artery affected. Nevertheless, a precise diagnosis may be difficult if secondary exudative manifestations are present or when preretinal, retinal, or subretinal hemorrhages cover the vessel anomaly. In those cases, angiography is indicated. Fluorescein angiography typically identifies that RAM as a round hyperfluorescent lesion along the course of a retinal artery, showing rapid filling of the lesion, and dye leakage throughout the study. When a thick hemorrhage is present, an area of blocked fluorescence around the aneurysm is observed. Indocyanine green angiography may reveal particularly useful in the identification of RAM in cases associated with thick hemorrhage, correctly guiding the laser treatment application. It is noteworthy that a dye leakage can be found even using indocyanine green angiography, revealing the damage to the artery wall.

OCT may unveil the presence of exudative manifestations, including blood, intraretinal cysts, neurosensory detachment, and at times small intraretinal breaks which are detectable on the external surface of neurosensory detachment.

Differential Diagnosis

Many conditions should be differentiated from RAM, including traumatic hemorrhage, branch retinal vein occlusion, idiopathic parafoveal telangiectasia, Leber's miliary aneurysm retinopathy, Coats' disease, radiation retinopathy, von Hippel-Lindau disease, capillary hemangioma, cavernous hemangioma, arteriovenous malformation, diabetic retinopathy, and exudative age-related macular degeneration.

Therapy

Treatment of RAM is controversial. At present there is no general consensus about the indications to the treatment of RAM. Spontaneous obliteration of RAM may occur over the follow-up, but the long persistence of blood or subretinal fluid may lead to progressive photoreceptor damage with consequent visual impairment. More specifically, long-standing subretinal hemorrhage beneath the fovea leads to a progressively impaired visual function. Treatment is generally indicated for symptomatic RAM, which is associated with exudative manifestations involving the fovea (Battaglia Parodi et al. 2011). The most commonly employed approach is direct or indirect laser photocoagulation with visible end point. Conventional laser treatment is generally affective in achieving the obliteration of RAM and the resolution of the exudative manifestations. Nevertheless, several complications may be associated with visible laser photocoagulation for any macular lesion, including enlargement of laser scar, choroidal neovascularization, and subretinal fibrosis. In addition to these complications, arteriolar obliteration, increased retinal exudation, and scarring, with possible retinal traction, have also been explicitly reported as potential sequelae of the conventional laser photocoagulation of RAM.

A different approach can be pursued with the use of subthreshold laser treatment, which minimizes the negative aspects of conventional photocoagulation by reducing the duration of laser exposure and by using a subvisible clinical end point. Subthreshold laser treatment can reach the same anatomical and functional outcomes obtained with conventional laser treatment, but generally requires more time to take affect (Battaglia Parodi et al. 2012).

Laser hyaloidotomy using neodymium-YAG, argon, or krypton lasers for the successful management of subhyaloid hemorrhage has been

reported, even though there is the risk of damage to the macula. In the setting of vitreous hemorrhage, or when the laser fails to induce blood evacuation into the vitreous cavity or the blood pocket is too close to the macula, vitreous surgery may be performed. Submacular hemorrhage can be surgically removed with the help of recombinant tissue plasminogen activator or with a combined approach with pneumatic displacement.

Intravitreal injection of anti-VEGF molecules can accelerate the progressive involution of the RAM, with faster resolution of the exudative manifestations.

Epidemiology

RAM usually develops in patients between 60 and 80 years of age, with higher prevalence in the female gender. Although usually singular and unilateral, RAM can be bilateral in 10% of cases and can also present with multiple aneurysms along the same vessel or on multiple vessels in 20% of cases. Systemic hypertension is the most commonly associated risk factor. Up to 75% of patients have a history of systemic hypertension and clinical or ophthalmoscopic evidence of arteriosclerosis (Rabb et al. 1988). Other risk factors reported in the literature include elevated lipid levels and systemic vasculitis such as polyarteritis nodosa, sarcoidosis, diabetes, rheumatoid arthritis, and Raynaud's phenomenon.

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Aneurysms

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Definition

An aneurysm is classically an abnormal area of dilation in the wall of an artery (but also can affect veins and the heart). A true aneurysm involves all three layers at an antery.

Etiology

There are a number of factors that impact the likelihood of having an aneurysm including trauma, family history of aneurysms, smoking, hypertension, atherosclerosis, syphilis, older age, and genetic conditions that weaken the connective tissue wall of the artery. Examples of genetic conditions that predispose to aneurysm are Marfan syndrome and Ehlers-Danlos syndrome. Aneurysms may be placed into the following categories: aortic aneurysms, brain aneurysms, or peripheral aneurysms. This section will mostly focus on cerebral aneurysms that may present with visual defects.

Cerebral Aneurysms

An intracranial aneurysm can affect any part of the cerebral circulation but typically occurs at the bifurcations. An aneurysm can rapidly expand and rupture producing an intracranial hemorrhage.

Clinical Presentation

The clinical presentation may vary based on the location of the aneurysm and whether or not a rupture has occurred. Patients who have an unruptured cerebral aneurysm may remain asymptomatic until the aneurysm expands to a very large size, impinges on an adjacent structure, causing focal neurologic or stroke-like signs, or ruptures.

Posterior Communicating Artery Aneurysms

Aneurysms at this location may cause an ipsilateral oculomotor nerve palsy because of the close proximity of the posterior communicating artery to the oculomotor nerve in the subarachnoid space. Basilar tip aneurysms might also cause third nerve palsy.

Internal Carotid Artery Aneurysms

Aneurysms at this location may cause compression in the cavernous sinus of ocular motor cranial nerves, or suprasellar lesions may cause compression of the optic nerve or optic chiasm, leading to visual acuity or visual field defects.

Anterior Cerebral Artery Aneurysms

Aneurysms at this location may cause compression of the optic chiasm or the optic nerve, depending on the direction in which the aneurysm extends.

Diagnostics

The usual method utilized to diagnose an aneurysm is neuroimaging. Cranial CT or MRI may be used for screening but in general angiography of some type is necessary for the evaluation of intracranial aneurysms. CT angiography (CTA) and MR angiography (MRA) are less invasive but less sensitive for the detection of aneurysm than standard catheter digital subtraction angiography (DSA).

Differential Diagnosis

On the differential for brain aneurysm are acute stroke, arteriovenous malformation, cerebral hemorrhage, cluster headache, hydrocephalus, and fibromuscular dysplasia.

Prophylaxis

Prophylactic measures are centered on reducing risk factors for developing an aneurysm by lifestyle alterations. Smoking cessation, adoption of a healthy diet, physical activity, and hypertension or hyperlipidemia control are the major methods to reduce risk.

Therapy

Aneurysms may be treated with either surgery, endovascular technique or medical management. Small asymptomatic or incidentally found aneurysms may not require treatment. Symptomatic, larger, or radiographically enlarging aneurysms may require endovascular therapy or surgical clipping depending on clinical circumstance.

Prognosis

The prognosis for patients who have an aneurysm depends on a number of factors and widely varies. Location of the aneurysm, whether or not the aneurysm has ruptured, and whether or not surgery or endovascular therapy is required are important prognostic factors.

Epidemiology

Cerebral aneurysms have an incidence of 2–5%, and up to 1.9% of these patients can experience rupture.

Cross-References

▶ Aneurysm Retinal Arterial

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Angiofibromas, Facial, in Tuberous Sclerosis

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Synonyms

Fibrous papule

Definition

Angiofibromas are tiny, smooth-surfaced papules that are found on the body. They are most commonly seen on the nose and the medial portions of the cheeks, but they may also be present on the chin, forehead, and eyelids. These papules are fibrous tissue composed of collagen and vascular elements of the skin and can vary in appearance, from red or flesh colored on light skin, to reddish brown and dark brown on more highly pigmented skin. While a single angiofibroma is most likely benign, the presence of multiple angiofibromas on the body may suggest that there is an underlying medical condition such as tuberous sclerosis ("adenoma sebaceum") Birt-Hogg-Dube syndrome, or multiple endocrine neoplasia type 1.

A majority of patients with tuberous sclerosis have multiple angiofibromas, which can range anywhere from as few as three to hundreds. Angiofibromas may occasionally be confused for basal cell carcinomas. In order to rule out the aforementioned diseases and determine the type of angiofibroma that is present, biopsy is typically needed. Treatment of an angiofibroma is centered on the lesion's destruction. Shave excision, dermabrasion, electrodessication and curettage, and laser therapy are some of the conventional options that are available for treatment. Recently, it was discovered that topical rapamycin can cause regression of facial angiofibromas and can lead to better cosmetic outcomes as well. After treatment, recurrence of the lesion is not uncommon. Of note, angiofibromas can be highly proliferative during puberty in both males and females. For this reason, if a child has an angiofibroma, treatment may be performed prior to pubertal age in order to prevent further growth from occurring.

Further Reading

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Angiography, Fluorescein

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Definition

Sodium fluorescein (molecular weight 376 Da) is an orange-red crystalline hydrocarbon that can absorb photons of light in the blue wavelength (465–490 nm) of light and subsequently emit them in the yellow-green wavelength (520–530 nm) of light (Gass 1997; Johnson et al. 2006) (Fig. 1).

Indication

Sodium fluorescein is used primarily as an intravenous diagnostic agent during ocular angiography to diagnose and treat ocular diseases affecting the retina and choroid. During ocular angiography, it effectively demonstrates the retinal circulation based on its ability to bind serum proteins and remain in the intravascular space following intravenous injection. It can also be used as a topical solution to identify epithelial defects on the corneal surface.

Contraindication

The main contraindication to the use of sodium fluorescein is a history of a severe allergic or anaphylactic reaction to fluorescein. It should be used with caution in patients with severe liver or kidney dysfunction, as its rate of drug clearance may be reduced.

Use and Dosage

During fluorescein angiography, sodium fluorescein is given intravenously as either 3 mL of a 25% concentration or 5 mL of a 10% concentration in a sterile aqueous solution immediately prior to obtaining photographs. For topical use, sodium fluorescein is administered as a 0.25% solution.

Adverse Reactions

Sodium fluorescein is a relatively safe drug but does cause a transient yellowing of the skin and conjunctiva for up to 12 h in all patients. It also produces a transient orange-yellow discoloration of the urine for up to 36 h in all patients. Less common systemic side effects include nausea, vomiting, and vasovagal reactions, which occur in up to 10% of patients. These symptoms can be mitigated in some patients by injecting the intravenous dye very slowly. If sodium fluorescein extravasates into surrounding dermal tissue during intravenous injection, it can produce a local inflammatory reaction which can rarely lead to tissue necrosis. Urticarial reactions occur in approximately 1% of the patients, with less than 1 in every 100,000 patients developing frank anaphylaxis or shock.

Angiography, Fluorescein, Fig. 1 Fluorescein angiography of the ocular fundus

Interactions

Major interactions between sodium fluorescein and other systemic medications are rare. However, free circulating levels of sodium fluorescein may be effectively increased for patients in a protein deficient state.

Cross-References

▶ Epithelial Defects
▶ Indocyanine Green

▶ Retina, Structure of
▶ Retinal Blood Vessels

References

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Angioid Streaks

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Synonyms

Knapp streaks or Knapp striae

Definition

Angioid streaks (AS) are irregular radiating jagged lines extending from the peripapillary area into the periphery with an ophthalmoscopic similarity to blood vessels. They result from breaks in calcified Bruch's membrane and may appear in numbers with atrophy in the surrounding area. Fifty percent of patients have associated systemic disorders that include pseudoxanthoma elasticum (PXE), osteitis deformans (Paget's disease), and various blood dyscrasias such as sickle cell anemia, fibrodysplasia hyperelastica (Ehlers-Danlos syndrome), and senile elastosis of the skin. Angioid streaks may lead to the development of choroidal neovascularization (CNV) and macular degeneration (Piro et al. 1983), which can cause severe vision loss.

Disease

Angioid streaks were first described by Doyne in a case presentation to the Ophthalmologic Society of the United Kingdom (Doyne 1889). In 1892, Knapp coined the term angioid streak. Kofler, in 1916, stated that the main changes were at the level of Bruch's membrane (Knapp 1892; Kofler 1917). Anatomopathological correlations by Bock in 1938 and Hagedoorn in 1939 in patients with pseudoxanthoma elasticum confirmed that the angioid streaks represent linear breaks in Bruch's membrane.

Etiology

Histopathologic studies of eyes with AS have shown linear partial breaks of the thickened and calcified Bruch's membrane. Subsequently, a full-thickness defect of Bruch's membrane may occur, followed by atrophy of the surrounding tissues or fibrovascular tissue ingrowth from the choroid. However, the reason why Bruch's membrane becomes calcified spontaneously or otherwise fragile and predisposed to developing cracks is unknown (Doyne 1889). A primary abnormality in the fibers of Bruch's membrane has been suggested to induce a tendency for metal salt deposits (Klein 1947). Significant deposition of calcium, not iron, at Bruch's membrane has been identified in immunohistochemistry and electron microscopy in sickle cell anemia (Jampol et al. 1987). Immunohistochemistry of CNV with AS has also shown calcium deposits in Bruch's membrane (Kazato et al. 2010). Abnormal calcification of elastic tissue is seen in other parts of the body in patients with pseudoxanthoma elasticum, as well as with Paget's disease, sickle hemoglobinopathies, and other systemic disorders (Piro et al. 1983).

Predisposition to AS is often idiopathic or associated with systemic conditions such as PXE, Paget's disease, sickle cell anemia, and Ehlers-Danlos syndrome.

Clinical Presentation

Typically, linear irregular streaks radiate outward from a peripapillary ring to the periphery on ophthalmoscopy. The streaks can be wide or narrow, tapering to a point within a few millimeters of the disk, and can vary in number. They lie deeper than the retinal vessels and have a cracked line appearance. The color of the angioid streaks can range from red to dark brown and generally depends on the pigmentation of the fundus and on the degree of overlying atrophy of the retinal pigment epithelium (RPE). They are almost always bilateral. AS may increase in length and width over time but do not regress. Spontaneous atrophy develops in the vicinity of the AS.

Other associated findings include *peau d'orange* changes, peripheral focal lesions (salmon spots), hemorrhages with or without scarring, and disk drusen that may classically precede the appearance of the streaks (Gass 1997). The peau d'orange term describes the fine, relatively symmetrical, widespread drusen-like, flat, yellowish, and occasionally confluent lesions at the level of the RPE. The mottled fundus appearance is most distinct in the area temporal to the macula but extends throughout the posterior pole and sometimes up to the equator. Visual acuity is not affected by peau d'orange even when the fovea is involved. When identified in an individual, siblings and parents should be investigated for the presence of peau d'orange even in the absence of angioid streaks.

Punctate or reticular macular pigment dystrophies may appear over time. "Comets" are multiple, small, subretinal white crystalline bodies, sometimes associated with a tail of RPE atrophy pointing toward the optic disk. Such comets are located in the fundus mid-periphery or juxtapapillary and are considered highly suggestive for PXE.

Other retinal changes follow focal or blot hemorrhages: salmon patches (typically the healing of subretinal hemorrhage), black dots (the result of metaplasia of the pigment epithelium), and "pearls" (deep white or yellow-white foci 150–300 μ in size, either resulting from subretinal or sub-RPE hemorrhage or from the spontaneous healing of a focal disciform scar). Occasionally, subretinal hemorrhages in the periphery, near the ora serrata, may evolve into discoid metaplasia of the RPE simulating disciform degeneration.

Although the exact prevalence is unknown, AS seem to appear more frequently in white people compared with Asians and black people (Dhermy 1987; Mansour et al. 1993) and can manifest at various ages depending on associated conditions.

Associated systemic disorders were found in half of the cases of angioid streaks using a diagnostic survey (Clarkson and Altman 1982). By far, the most common is PXE (Grönblad-Strandberg syndrome), followed by Paget's disease and sickle hemoglobinopathies. Many other conditions have been reported (Clarkson and Altman 1982) (Table 1).

PXE is a rare autosomal recessive inherited multisystem disease, with mutations in the ABC transporter gene *ABCC6* on chromosome 16 encoding for cellular transport protein, which are responsible for the disease. The basic defect in PXE may be glycosaminoglycans and glycoproteins attached to elastic fibers that cause abnormal collagen synthesis.

PXE affects 1 in 25,000–100,000 people. Angioid streaks are present in approximately 85% of patients with PXE with a variable phenotype (Knapp 1892; Ellabban et al. 2012). They may already be seen in young adults and develop in almost all patients with time (Georgalas et al. 2009). Other ocular associations more commonly noted in cases associated with PXE include

Angioid Streaks, Table 1 Common systemic conditions associated with angioid streaks

Finding	%
PXE	30–50
Paget's disease	10
Hemoglobinopathy	6
Idiopathic	50

optic disk drusen, salmon spots, and peau d'orange.

Paget's disease is a chronic, progressive, sometimes hereditary connective tissue disorder that involves the collagen matrix of the bone. The most significant mutation identified is in the nuclear factor B signaling pathway. In advanced Paget's disease, angioid streaks develop in 10–15% of patients. The incidence is greater in those patients with early onset of symptoms, skull involvement, and an active systemic disease as demonstrated by markedly elevated serum alkaline phosphatase and urinary hydroxyproline.

Angioid streaks appear in 1–20% of patients with any of the hemoglobinopathies, with the incidence increasing with age. The incidence is not related to the degree or stage of proliferative sickle cell retinopathy. Complications, such as CNV or macular degeneration, are uncommon.

Angioid streaks have been found in patients with the Ehlers-Danlos syndrome – a rare autosomal dominant connective tissue disorder with hyperextensible skin and hyperflexible joints caused by an abnormality in the synthesis and metabolism of collagen. Senile elastosis with angioid streaks is considered rare. The other systemic conditions described probably represent coincidental findings.

Diagnosis

Most patients with angioid streaks are asymptomatic unless the macula is involved. Thus, the initial diagnosis is often made on routine ophthalmoscopic examination. In at risk families, a screening examination will reveal characteristic features of AS. However, decrease of vision due to a subretinal hemorrhage after a mild head or eye contusion occurs in up to 15% of patients with AS. The most common and significant complication of AS is the development of CNV.

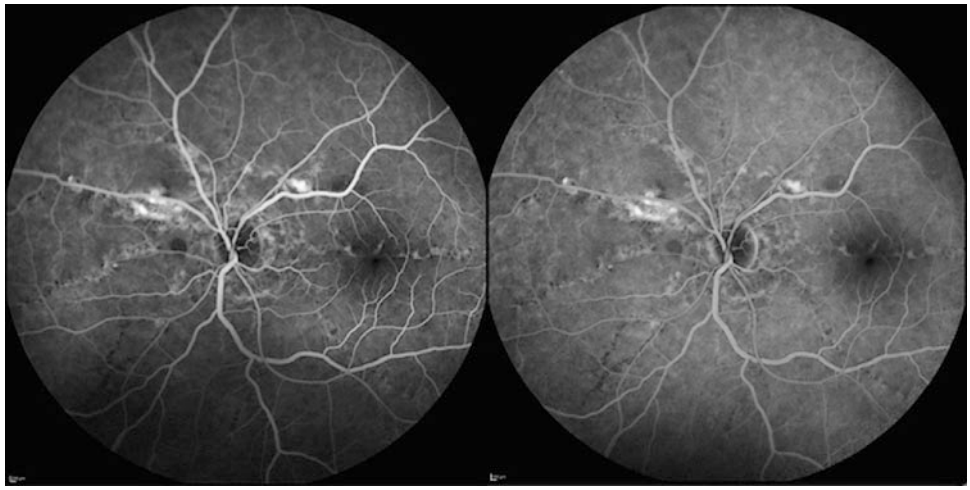
The initial diagnosis of AS requires a diagnostic workup for a systemic disease in the patient but also in the family. PXE has an autosomal recessive inheritance, whereas Ehlers-Danlos syndrome and Paget's disease are autosomal dominant. Senile elastosis, sickle cell disease, facial angiomatosis, and neurofibromatosis also have familial occurrence.

Diagnostic Tests

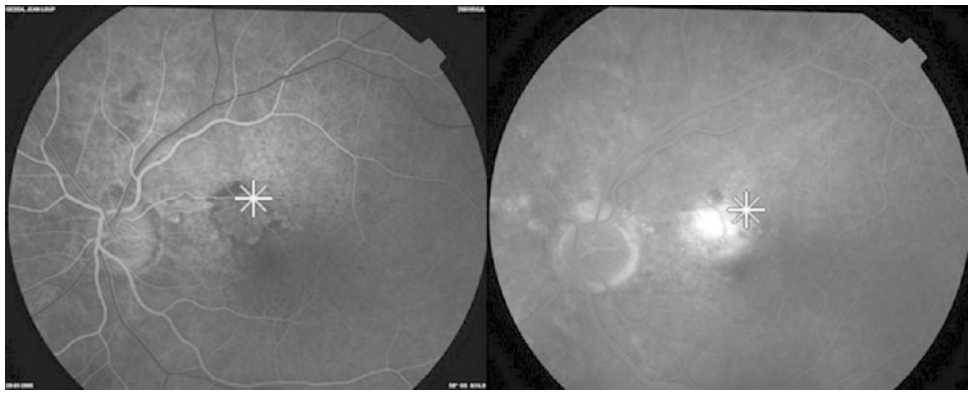
The diagnosis is usually made by clinical examination alone. Fluorescein angiography (FA) confirms or ascertains the diagnosis when the clinical findings are subtle or uncertain. In addition, FA is a critical tool as part of the evaluation in any patient with angioid streaks and visual symptoms to identify associated CNV, which would warrant therapy. Occasionally, FA findings may reveal a streak under CNV that is not clinically observed. Angioid streaks appear irregularly hyperfluorescent on FA due to overlying RPE atrophy with mottled edges from RPE clumping (Fig. 1). The choroidal neovascular membrane usually arising from the border of a macular streak will show a characteristic increase in size and intensity of fluorescence with angiography progression of pre-epithelial CNV, for example, located between the RPE and the photoreceptor the layer (Fig. 2; Nakagawa et al. 2013). Fundus autofluorescence, which is considered to reflect the RPE metabolic activity, varies in relation with the severity of atrophy.

On indocyanine green angiography, angioid streaks are hyperfluorescent on early-phase angiograms (Fig. 3). On late frames, the streaks located at the posterior pole are hyperfluorescent, while those eccentric demonstrate a normal fluorescence. The peau d'orange, rarely visible on FA, stains in a speckled pattern mainly temporal of the macula.

Spectral-domain optical coherence tomography (OCT), which allows for quasi-histologic assessment of the posterior ocular fundus in vivo, has been used to study PXE-related features. Angioid streaks have consistently been found to be associated with breaks in Bruch's membrane, providing the clinical direct evidence of the underlying pathology of AS (Finger et al. 2010). The calcification of Bruch's membrane may induce an increased reflectivity (Fig. 4). Disruption and undulation (inward and outward deformation) of Bruch's membrane on



Angioid Streaks, Fig. 1 Fluorescein angiography of LE with angioid streaks. Early and late phase showed an early central zone of hypofluorescence due to a break in Bruch's membrane, causing a separation of the choriocapillaris. Adjacent light-colored areas were hyperfluorescent, possibly due to abnormal retinal pigment



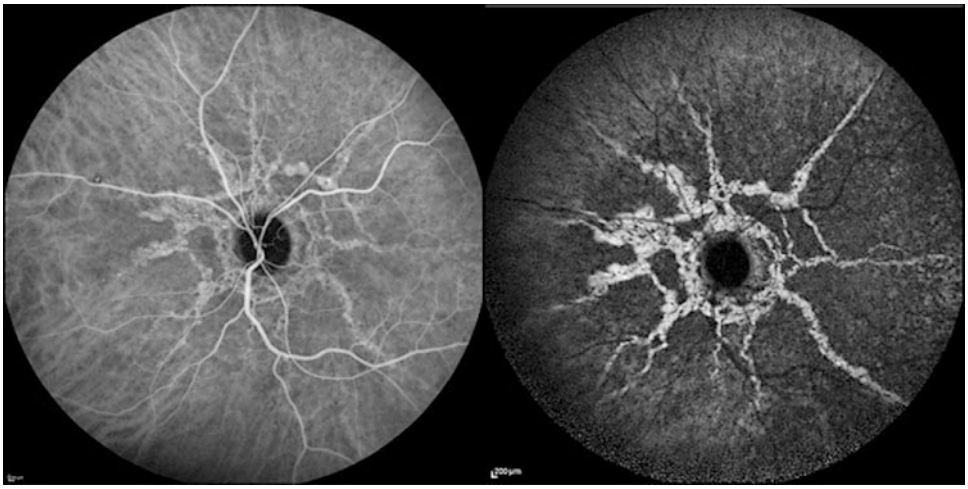
Angioid Streaks, Fig. 2 The left eye at baseline. Early and late phase of fluorescein angiography showed leakage from active subfoveal choroidal neovascularization secondary to angioid streak

OCT are much more frequent in eyes of older PXE patients than in eyes of AMD patients (Connor et al. 1961), adding a clue to differentiate between those two causes for CNV. The transition from calcified to uncalcified retinal areas correlates well with peau d'orange changes (Fig. 5; Finger et al. 2010). Comet tails, which are difficult to record due to their localization, may show hyporeflective spaces in the outer neurosensory retina with a slightly hyperreflective inner lining and focal debris-like deposits just above the RPE level (Finger et al. 2010). Mean subfoveal choroidal thickness is reduced (Gliem et al. 2014).

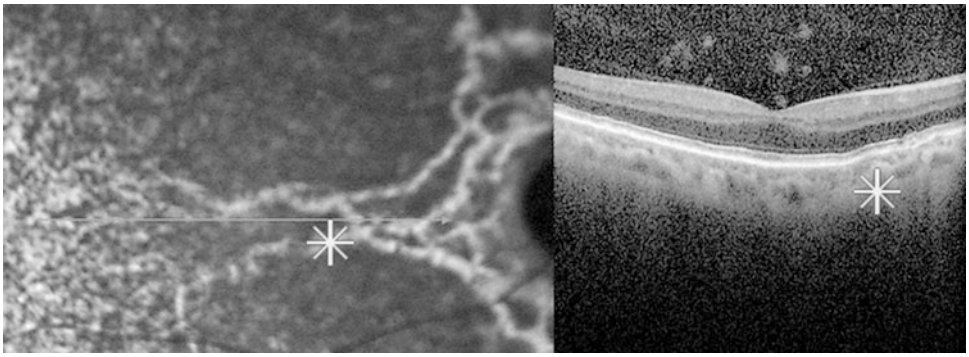
Secondary Complications

AS can cause subretinal hemorrhages from choroidal fibrovascular ingrowth that may spread toward the macula. These hemorrhages can resolve spontaneously. In addition, extensive calcification of Bruch's membrane and AS may progress to severe CNV and disciform scarring.

An estimated 72–86% of patients with AS have CNV at presentation (Connor et al. 1961; Mansour et al. 1988). A British study reported AS-associated CNV affecting mostly young or middle-aged individuals and occurring at an incidence of 0.057 per 100,000 people (Abdelkader



Angioid Streaks, Fig. 3 ICG angiography frames of the left eye. Angioid streaks are hyperfluorescent on early- and late-phase ICG angiogram



Angioid Streaks, Fig. 4 Optical coherence tomography of the left eye. *Asterisks* indicate corresponding angioid streaks on indocyanine green angiogram and on spectral-domain optical coherence tomography. Increased reflectivity is seen within the outer zone of retinal pigment epithelium-Bruch's membrane complex and disruption in the photoreceptor layer

et al. 2013). Pre-epithelial CNV usually occurs on the borders of the streaks in the posterior pole. Occasionally, eccentric CNV may remain unnoticed because of the low impact on visual function. CNV leads to subretinal hemorrhage and exudation and results in the formation of a fibrovascular scar. Overall, classic CNV appears to have a worse spontaneous prognosis with regard to visual function compared to sub-epithelial CNV that is rare in AS (Nakagawa et al. 2013). CNV can be recurrent and lead to progressive visual loss, especially in middle-aged active patients.

Recently, polypoidal choroidal vasculopathy (PCV) was also described in eyes with angioid streaks (Nakagawa et al. 2013). In contrast to classic CNV, these polyps are not located next to the angioid streak. PCV may occur as an initial vascular change or secondary to CNV.

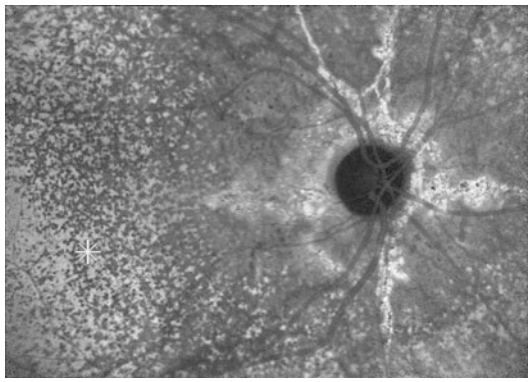
Differential Diagnosis

For differential diagnosis, consider exudative age-related macular degeneration (AMD), choroidal rupture and choroidal folds, toxoplasmosis,

histoplasmosis, retinal vasculitis, myopia and lacquer cracks, choroidal sclerosis, and traumatic subretinal hemorrhage.

Prophylaxis

Initially, patients are mostly asymptomatic and should be advised to wear safety glasses and to avoid contact sports, which could increase the potential risk of subretinal hemorrhage even from relatively mild ocular contusion. Prophylactic photocoagulation treatment of the AS should not be performed as it may induce CNV. Genetic counseling should be considered in some cases.



Angioid Streaks, Fig. 5 Asterisk in ICG angiography indicates the area of peau d'orange, which is characterized by *small dark spots* on a whitish or opaque background (calcified and noncalcified Bruch's membrane)

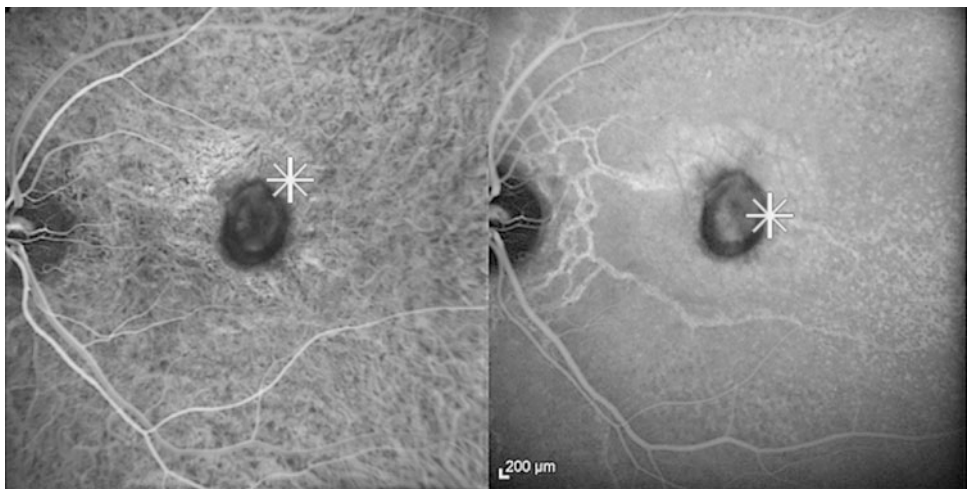
Prognosis

The visual prognosis of eyes harboring angioid streaks depends on the ingrowth of choroidal neovascularization. Subsequent macular degeneration can cause devastating visual loss, especially when bilateral, often leading to visual acuity of 20/200 or worse. Vital prognosis depends on the associated systemic diseases that may be life threatening.

Treatment

Historically, CNV associated with AS has been successively treated with laser photocoagulation, photodynamic therapy with verteporfin, or surgery in short term; however, all developed disappointing functional and long-term results (Pece et al. 1997; Roth et al. 2001).

Recently, some studies have shown the benefits of intravitreal injections of anti-vascular



Angioid Streaks, Fig. 6 At 12-month follow-up after four injections of ranibizumab, indocyanine green angiography confirmed resolution of choroidal neovascularization activity despite persistence of a well-defined, inactive neovascular network, indicated with *asterisk*

endothelial growth factor (VEGF) in small series using bevacizumab (Bhatnagar et al. 2007; Myung et al. 2010). A large retrospective case series showed stabilization of visual acuity using ranibizumab (Mimoun et al. 2010). Ranibizumab is another anti-VEGF agent approved by the FDA for the treatment of all types of CNV due to AMD.

Due to the multiple breaks in Bruch's membrane, CNV may persist, compelling continuous and frequent follow-up of both eyes both during and after treatment periods. Figure 6 demonstrates a case of CNV treated repeatedly with ranibizumab, resulting in an inactive neovascular network after 12 months. Currently, treatment is aimed at slowing the progression of vision loss and recurrence of CNV.

Cross-References

- ▶ Choroidal Neovascularization
- ▶ Ranibizumab

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Angioid Streaks – Ehlers-Danlos Syndromes

▶ Ehlers-Danlos Syndrome, Angioid Streaks in

Angiomas (Angiomatosis)

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Definition

An angioma is a benign tumor composed of cells of the vascular or lymphatic system. Angiomas can be various in shapes and sizes and present in individuals as they age. The presence of an angioma does not necessarily indicate an underlying disorder. The presence of multiple angiomas, however, is highly suspicious for a systemic disease process. Angiomas can develop on any part of the body, but they are commonly seen close to the skin surface and may cause skin discoloration or nodules. Angiomas can be classified into two groups: hemangiomas if they are derived from cells of the vascular system and lymphangiomas if they are derived from cells of the lymphatic system. The majority of angiomas are harmless and may be left untreated unless they are causing damage to the adjacent tissue. However, retinal angiomas may be a cause for concern because they can involve prominent arterioles or venules of the eye and might suggest von Hippel-Lindau disease.

Angiomatosis is a benign medical condition in which there are multiple angiomas throughout the body, on the skin, or internal organs. One of the notable risks that come with multiple angiomas is that they may rupture and cause internal bleeding. Angiomatosis is associated with a number of diseases, including Von Hippel-Landau disease, bacillary angiomatosis, Klippel-Trenaunay-Weber syndrome, and Sturge-Weber syndrome. Retinal angiomatosis is the most common presenting feature of von Hippel-Lindau disease. Angiomatosis may also be acquired as a result of Bartonella infection, which typically occurs in immunodeficient individuals. This condition is known as bacillary angiomatosis.

Cross-References

▶ Klippel-Trenaunay-Weber Syndrome
▶ Port-Wine Stain (Nevus Flammeus) in Sturge-Weber Syndrome
▶ Retinae (Retinal Angiomatosis, von Hippel Syndrome/Disease)

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Angiomatosis Retinae

▶ Hemangioblastomas, with Retinal Angiomatosis (von Hippel Lindau Disease)
▶ Retinae (Retinal Angiomatosis, von Hippel Syndrome/Disease)
▶ VHL Syndrome

Angioosteohypertrophy Syndrome

▶ Klippel-Trenaunay-Weber Syndrome

Angle Closure

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Synonyms

Closed angle

Definition

Angle closure is defined by iridotrabecular contact, followed by reduced outflow of aqueous humor through the anterior chamber angle. Angle closure can occur due to reversible apposition of the peripheral iris to the trabecular meshwork (*acute angle closure*) or due to irreversible peripheral anterior synechiae (PAS) (chronic angle closure). The term *angle-closure glaucoma* is used if glaucomatous optic neuropathy (GON) is present.

Etiology

Angle closure is caused either by anterior ("pulling") or posterior ("pushing") mechanisms, eventually leading to iridotrabecular contact.

In posterior "pushing" mechanisms, the iris is pushed forward from behind due to obstruction of aqueous flow at different anatomical locations: at the level of the pupil with absolute or relative pupillary block (*primary angle closure*, *acute angle closure*), at the level of the iris and ciliary body (*plateau iris configuration*, *plateau iris syndrome*), at the level of the lens (*phacomorphic glaucoma*, *lens-induced angle-closure glaucoma*), or posterior to the lens inducing forward movement of the lens-iris diaphragm (*aqueous misdirection*, *malignant glaucoma*, *uveal effusion*, retinal gas or oil tamponade, tumors, contracture of retrolenticular tissue in *retinopathy of prematurity* and *persistent hyperplastic primary vitreous*). Two or more mechanisms may coexist, although one is usually predominant.

In anterior ("pulling") mechanism, the iris is pulled forward into contact with the trabecular meshwork, either by consolidation of inflammatory products in the anterior chamber angle (*uveitic glaucoma*) or by contracture of membranes in the anterior chamber. Such membranes can be neovascular (in proliferative vitreoretinopathy, *central retinal vein occlusion*, *carotid occlusive disease*, *ocular ischemia*, or chronic retinal detachment), endothelial (in *ICE syndrome* or *posterior polymorphous dystrophy)*, or epithelial (after penetrating trauma or surgery).

The term primary refers to a condition where an anatomic predisposition without any further pathology leads to obstruction of aqueous flow and subsequent angle closure; the term secondary is used if an underlying pathologic cause for obstruction can be identified.

Chronic angle closure may develop after acute angle closure in which synechial closure persists. It may also develop when the anterior chamber angle closes gradually and intraocular pressure (IOP) rises slowly. In such cases, the term creeping angle closure may be used. In chronic or creeping angle closure, slowly, peripheral anterior synechiae advance circumferentially. Multiple "pushing" mechanisms may be involved, including pupillary block, iris changes, and plateau iris configuration.

Clinical Presentation

Most angle closures occur asymptomatically.

A shallow anterior chamber may be a hint at an occludable (or narrow) anterior chamber angle with possible angle closure either primarily in predisposed eyes (*angle-closure suspect*) or secondary to other pathologies.

Manifest angle closure can present as *acute angle closure* with excessive rise in IOP and severe symptoms, like decreased vision, halos, pain in the eye, headache, nausea, and vomiting, or as subacute or intermittent angle closure with mild recurrent symptoms like painless blurry vision. Thus, the sensitivity and specificity of symptoms for identifying angle closure are rather poor.

Signs of previous attacks include a permanently fixed and dilated pupil, sector iris atrophy,

pigmentary dusting of the corneal endothelium, anterior subcapsular lens opacities (so-called glaukomflecken), PAS, and manifest GON.

In chronic or creeping angle closure, PAS cause chronic but modest, asymptomatic elevation of IOP and eventually progressive GON with corresponding visual field defects.

Diagnosis

Angle closure is diagnosed on *gonioscopy*, preferably by indentational gonioscopy, to distinguish between appositional angle closure and PAS. *Ultrasound of the anterior segment* may reveal underlying structural changes of the peripheral iris or ciliary body. Biomicroscopy with accurate assessment of the anterior chamber as well as the posterior segment is mandatory in classifying the various forms of angle closure and angle-closure glaucoma.

Previous ocular and medical history, family history, as well as subjective symptoms should be inquired, and IOP measurements, visual field examination, retinal nerve fiber layer, and optic disk imaging should be performed to assess the stage of disease.

Differential Diagnosis

Shallow anterior chamber without angle closure

Therapy

Treatment varies depending on the etiology of angle closure and the clinical presentation (*acute angle closure*).

In intermittent and chronic angle closure, a laser iridotomy may be the treatment of choice to relieve a pupillary block component and to reduce the risk of further permanent synechiae. In some cases, the disease may nevertheless progress, and the long-term use of topical hypotensive medication or even filtering surgery may be indicated to lower IOP. In *secondary angle-closure glaucoma*, the underlying pathology should be eliminated.

Prognosis

Prognosis depends on the etiology of angle closure and the presence or absence of subsequent damage like GON.

Epidemiology

The prevalence for primary angle closure in populations older than age 40 varies depending on the ethnicity and is highest in Inuit, followed by East Asians and Japanese. Chronic angle closure is more common in black populations.

Cross-References

- ▶ Acute Angle Closure
- ▶ Altitudinal Visual Field Defects
- ▶ Angle Closure Secondary to Uveal Effusion
- ▶ Angle-Closure Glaucoma
- ▶ Angle-Closure Suspect
- ▶ Biomicroscopy, Ultrasound, of Anterior Segment
- ▶ Central Retinal Vein, Occlusion of
- ▶ ICE Syndrome
- ▶ Iris Defect
- ▶ Lens-Induced Angle-Closure Glaucoma
- ▶ Malignant Glaucoma
- ▶ Neovascular Glaucoma in Ocular Ischemia, Others
- ▶ Persistent Hyperplastic Primary Vitreous
- ▶ Phacomorphic Angle-Closure Glaucoma
- ▶ Posterior Amorphous Corneal Dystrophy
- ▶ Primary Angle Closure
- ▶ Retinopathy of Prematurity
- ▶ Secondary Angle-Closure Glaucoma
- ▶ Uveitic Glaucoma

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Angle Closure Secondary to Uveal Effusion

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Synonyms

Secondary angle closure glaucoma and uveal effusion

Definition

Uveal effusion is defined by escape of fluid to the choroid and to the potential space between choroid and sclera. This fluid accumulation and forward bowing of the choroid causes a mass effect, resulting in anterior displacement of the lens-iris diaphragm. Eventually, the anterior chamber is flattened and angle closure occurs due to iris apposition to the trabecular meshwork.

Etiology

Uveal effusion is not one clinical entity, but due to a variety of causes.

Idiopathic uveal effusion syndrome is a rare condition with spontaneous choroidal detachment typically in healthy middle-aged men, presumably due to a congenital scleral anomality with abnormal uveoscleral protein transport.

Uveal effusion may also occur secondary to impair of the venous or transscleral outflow. This includes uveal effusion due to inflammation in posterior *scleritis, posterior uveitis,* or in HIV, as well as uveal effusion due to congestion or increased choroidal venous pressure as seen in *nanophthalmos*, after scleral buckling procedures (especially encircling bands), after panretinal laser coagulation, but also in case of *central retinal vein occlusion* and arteriovenous communication.

Uveal effusion is also seen secondary to choroidal tumors. In rare cases, bilateral uveal effusion has been described after systemic medication with either Topiramate or Acetazolamide.

Irrespective of the underlying pathology, uveal effusion is associated with swelling of the ciliary body and anterior rotation of the ciliary body, and subsequent anterior displacement of the lens-iris diaphragm, resulting in anterior chamber flattening and appositional angle closure. Reduced outflow of aqueous results in elevated intraocular pressure (IOP); depending on how long the iridotrabecular contact persists, subsequent glaucomatous damage of the optic nerve head may be seen.

Clinical presentation

One or both eyes may be affected.

A shallow anterior chamber is present, and *angle closure* is verified on gonioscopy.

IOP is elevated; depending on the level of increase, pain, red eye, and blurry vision may be present.

A choroidal thickening and elevation of various degrees is present; often the ora serrata can be visualized without indentation.

A serous retinal detachment with shifting fluid is not uncommon; involvement of the fovea is the main cause of vision loss.

Diagnosis

Angle closure is diagnosed on *gonioscopy*

A significant difference in anterior chamber depth is suggestive of *secondary angle closure glaucoma*.

Ultrasound of the anterior segment may reveal ciliary body swelling and anterior rotation of the ciliary body.

B-scan *ultrasound biomicroscopy* reveals a smooth, convex, elevated membrane limited in the equatorial region by vortex veins and anteriorly by the scleral spur, usually thicker and less mobile than retina.

Tonometry reveals elevated IOP.

Biomicroscopy with accurate assessment of the anterior chamber as well as the posterior

segment is mandatory to identify the underlying cause of uveal effusion.

Refraction and axial length should be measured in patients with suspected idiopathic uveal effusion syndrome or nanophthalmos.

Previous ocular and medical history should be inquired.

Differential Diagnosis

For differential diagnosis of angle closure glaucoma, consider any secondary angle closure with elevated IOP, either neovascular glaucoma, *uveitic glaucoma*, *lens-induced angle closure*, and angle closure due to aqueous misdirection (*malignant glaucoma*).

Choroidal melanoma, multifocal atypical *central serous retinopathy*, and *Vogt-Koyanagi-Harada* disease can also produce choroidal elevation.

Prophylaxis

No prophylaxis is known for angle closure glaucoma secondary to idiopathic uveal effusion.

Therapy

Treatment is on the one hand directed at lowering IOP directly, but on the other hand the underlying mechanism causing uveal effusion should be targeted.

Beside topical hypotensive medication to lower IOP, cycloplegic agents can help deepen the anterior chamber by relaxing the ciliary body. To prevent peripheral anterior synechiae (PAS) in shallow anterior chamber, topical steroids should be administered.

Depending on the underlying cause of uveal effusion, anti-inflammatory therapy may be necessary, as well as drainage of suprachoroidal fluid, or surgical revision of a preceding scleral buckling procedure. In idiopathic uveal effusion, lamellar sclerectomy or sclerostomy may be necessary.

As angle closure secondary to uveal effusion is not associated with a pupillary block mechanism, an iridotomy is not indicated.

Prognosis

Prognosis depends on the etiology of uveal effusion. In most cases, angle closure resolves under correct treatment.

Epidemiology

Idiopathic uveal effusion is usually seen in middle-aged men.

Cross-References

- ▶ Angle Closure
- ▶ Biomicroscopy, Ultrasound, of Anterior Segment
- ▶ Central Retinal Vein, Occlusion of
- ▶ Choroidal and/or Ciliary Body and/or Iris Melanoma
- ▶ High-Resolution Ultrasound Biomicroscopy
- ▶ Idiopathic Central Serous Retinopathy/ Chorioretinopathy
- ▶ Lens-Induced Angle-Closure Glaucoma
- ▶ Malignant Glaucoma
- ▶ Nanophthalmos
- ▶ Posterior Vitreous Detachment
- ▶ Scleritis
- ▶ Secondary Angle-Closure Glaucoma
- ▶ Uveitic Glaucoma
- ▶ Vogt Lines, Keratoconus

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Angle Recession Glaucoma

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Synonyms

Postcontusion glaucoma

Definition

Angle recession glaucoma is a chronic secondary open-angle glaucoma due to a blunt ocular trauma (Blanton 1964; Kaufman and Tolpin 1974; Stamper et al. 2009).

Etiology

Blunt ocular trauma may cause a tear in the ciliary muscle (angle recession). The angle recession itself is not the cause of the glaucoma. It is rather an indicator of previous trauma to the eye resulting in a chronic pressure rise (Blanton 1964; Kaufman and Tolpin 1974; Stamper et al. 2009). Eyes with an underlying tendency for primary open-angle glaucoma are more likely to develop chronic angle recession glaucoma (Stamper et al. 2009).

Clinical Presentation

The onset of a chronic, initially mild to moderate elevation of intraocular pressure might be delayed for months to years (Blanton 1964; Kaufman and Tolpin 1974; Stamper et al. 2009). Chronic angle recession and primary open-angle glaucoma show similar clinical course and treatment (Blanton 1964; Kaufman and Tolpin 1974; Stamper et al. 2009).

Diagnosis

Angle recession is diagnosed by gonioscopy and/or ultrasound biomicroscopy (UBM) (Stamper et al. 2009):

Angle Recession Glaucoma, Fig. 1 On gonioscopical examination an irregular widening of the ciliary band is visible. Sometimes carefully gonioscopy and comparison of both eyes is necessary to detect the changes

- Angle recess might be gonioscopically visible as an irregular widening of the ciliary band (Fig. 1).
- Posterior attachment of the iris root.
- Deep anterior chamber (deeper than in the fellow eye).
- Visible glistening scleral spur (Stamper et al. 2009).
- Torn or absent iris processes.
- Posterior anterior synechiae (PAS) at the border of recession and normal iris root.
- Increased visibility and width of the scleral spur.

However, postcontusion glaucoma may present with variable gonioscopic findings from severe-angle recession to very mild or even absent anatomical abnormalities (Blanton 1964; Kaufman and Tolpin 1974; Stamper et al. 2009).

Differential Diagnosis

Primary open-angle glaucoma, steroid-response glaucoma.

Prophylaxis

Since late onset of pressure rise is possible even years or decades after the initial injury, annual checkups are advisable (Blanton 1964; Kaufman and Tolpin 1974; Stamper et al. 2009).

Therapy

Local antiglaucomatous drugs are the first-line therapeutical regimen (Stamper et al. 2009). Laser trabeculoplasty is often disappointing and of limited use (Stamper et al. 2009). Filtration surgery is an alternative when medical therapy fails (Stamper et al. 2009).

Prognosis

Similar to open-angle glaucoma.

Epidemiology

The risk of developing angle recession glaucoma is 2–10% in eyes after blunt trauma (Blanton 1964; Kaufman and Tolpin 1974; Stamper et al. 2009).

Cross-References

- ▶ Blunt Trauma
- ▶ Traumatic Glaucoma

Further Reading

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Angle-Closure Glaucoma

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Synonyms

Narrow-angle glaucoma

Definition

The term angle-closure glaucoma defines a condition in which elevated intraocular pressure (IOP) due to ▶ angle closure has caused glaucomatous optic neuropathy (GON) and corresponding ▶ visual field defects, although elevation of IOP or peripheral anterior synechiae (PAS) may be absent at the time of initial examination.

Etiology

Primary angle closure occurs in predisposed but otherwise normal eyes, whereas secondary angle closure is due to an identifiable underlying pathology (▶ primary angle closure and angle-closure glaucoma, secondary angle-closure glaucoma).

Irrespective of primary or secondary, ▶ angle closure is caused either by anterior ("pulling") or posterior ("pushing") mechanisms, both of which eventually leading to iridotrabecular contact either due to transient apposition of the iris to the trabecular meshwork or due to irreversible PAS (▶ angle-closure suspect).

In either mechanism, outflow of aqueous humor through the anterior chamber angle is reduced, resulting in acute, intermittent or chronic, moderate to excessive, elevation of IOP, thus eventually causing angle-closure glaucoma characterized by GON and corresponding visual field defects.

Besides the above-described mechanism of direct obstruction, often with rapidly developing PAS, aqueous outflow may also be impaired by irreversible degeneration and damage of the trabecular meshwork during phases of raised IOP.

PAS in chronic angle closure may develop after an acute attack in which synechial closure persists, or may also develop when the chamber angle closes gradually with slow formation of PAS, which advance circumferentially. In such creeping ▶ angle closure, multiple mechanisms are suspected to be involved, including pupillary block and ▶ plateau iris.

Clinical Presentation

Most angle closures occur asymptomatic.

A shallow anterior chamber may be a hint at a narrow anterior chamber angle with possible angle closure. Asymmetry of anterior chamber depth is typical in secondary angle-closure glaucomas. Peripheral anterior synechiae are usually present.

Despite the varying degree of clinical symptoms of acute elevation of IOP (▶ acute angle closure), patients with angle-closure glaucoma show GON and corresponding retinal nerve fiber layer and ▶ visual field defects.

Additionally, signs of previous acute angle-closure attacks, including a mid-dilated pupil, sector iris atrophy, pigmentary dusting of the corneal endothelium, and anterior subcapsular lens opacities (so-called glaukomflecken), may be present.

Diagnosis

▶ Angle closure is diagnosed on gonioscopy.

Dynamic gonioscopy enables to distinguish between appositional angle closure and PAS.

Tonometry usually reveals elevated IOP, although in some cases IOP may be within normal limits at the time of examination.

Biomicroscopy with accurate assessment of the anterior chamber is necessary for the classification of angle-closure glaucoma. A significant difference in anterior chamber depth is suggestive of ▶ secondary angle-closure glaucoma.

Assessment of the posterior segment is mandatory to detect glaucomatous changes of the optic nerve and retinal nerve fiber layer, as well as for the classification of angle closure secondary to mechanisms behind the iris/lens diaphragm.

Previous ocular and medical history, family history, as well as subjective symptoms should be inquired to exclude or confirm previous attacks of angle closure.

▶ Visual field examination, retinal nerve fiber layer assessment, and optic disk imaging should be performed to assess the stage of disease.

Differential Diagnosis

With respect to the treatment modalities, effort should be made to determine primary or secondary mechanisms of angle closure.

Consider neovascular glaucoma, ▶ uveitic glaucoma, ▶ lens-induced angle closure, and angle closure due to aqueous misdirection (▶ malignant glaucoma) or to choroidal pathologies (e.g., ▶ uveal effusion).

Also consider any ▶ secondary open-angle glaucoma with acute rise of IOP-like inflammatory, ▶ corticosteroid glaucoma, ▶ Posner-Schlossman syndrome, ▶ pseudoexfoliative glaucoma, ▶ pigmentary glaucoma, ▶ ghost cell glaucoma, phacolytic glaucoma, or open-angle glaucoma due to intraocular malignant tumors.

For differential diagnosis, also consider other causes for optic neuropathy like vascular (▶ anterior ischemic optic neuropathy) or compressive (▶ compressive optic neuropathy) mechanisms.

Prophylaxis

There is clear evidence for prophylactic treatment in fellow eyes of acute angle closure.

In intermittent and chronic angle closure, further angle closure should be avoided by reducing the risk of pupillary block.

Therapy

Therapy of angle-closure glaucoma depends on the etiology, clinical presentation, and stage of disease. In secondary angle-closure glaucoma, the underlying pathology has to be treated.

The aim of treatment is to prevent the further development of PAS and further glaucomatous damage due to elevated IOP. Medical treatment includes mild topical miotic agents, topical hypotensive medication like ▶ beta-blocker, ▶ alpha agonists, ▶ carbonic anhydrase inhibitors, and ▶ prostaglandin analogues.

Further treatment includes ▶ iridotomy (either laser or surgical) to relieve a pupillary block component and reduce the risk of further permanent synechiae. Despite a patent iridotomy, the disease may progress, and filtering surgery may be indicated to lower IOP.

Another approach is ▶ cataract surgery, especially in cases where a lens block mechanism is involved.

Prognosis

Angle-closure glaucoma accounts for 50% of all glaucoma blindness worldwide and is probably the most visually destructive form of glaucoma. Prognosis depends on the etiology, clinical manifestation, and stage of disease.

Prognosis for intermittent and chronic primary angle closure depends on the extent of optic nerve damage and subsequent IOP control.

Epidemiology

Prevalence of angle closure varies depending on the ethnicity and is highest in Inuit, followed by East Asians and Japanese. Chronic angle closure is more common in black populations.

Cross-References

- ▶ Altitudinal Visual Field Defects
- ▶ Angle Closure
- ▶ Angle Closure Secondary to Uveal Effusion
- ▶ Angle-Closure Suspect
- ▶ Corticosteroid
- ▶ Ghost Cell Glaucoma
- ▶ Iris Coloboma
- ▶ Lens-Induced Angle-Closure Glaucoma
- ▶ Malignant Glaucoma
- ▶ Nonarteritic Anterior Ischemic Optic Neuropathy
- ▶ Optic Neuropathy
- ▶ Pediatric Glaucoma
- ▶ Peripheral Retina
- ▶ Pigmentary Glaucoma
- ▶ Posner-Schlossman Syndrome
- ▶ Primary Angle Closure and Angle Closure Glaucoma
- ▶ Pseudoexfoliative Glaucoma
- ▶ Secondary Angle-Closure Glaucoma
- ▶ Secondary Open-Angle Glaucoma
- ▶ Uveitic Glaucoma

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Angle-Closure Suspect

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Synonyms

Anatomically narrow drainage angle; Narrow angle; Primary angle closure suspect

Definition

Angle closure suspects are individuals with two or more quadrants of appositional iridotrabecular contact on gonioscopy but without evidence of peripheral anterior synechiae (PAS), elevation of intraocular pressure (IOP), or glaucomatous optic neuropathy (GON).

Etiology

Typically in patients with small, "crowded" anterior segments, a shallow anterior chamber, and short axial lengths, this anatomic predisposition results in partial apposition of the iris to the trabecular meshwork. The risk of such iridotrabecular contact in an eye with a narrow anterior chamber increases when the angle between the iris and trabecular meshwork is

equal to or less than 20°. In contrast to ▶ acute angle closure, in angle closure suspects, iris apposition does not result in elevated IOP or any other clinical symptoms. Angle closure in predisposed subjects may be induced by various factors including drugs with sympathomimetic or parasympatholytic activity, pain, or emotional upset. (▶ mydriasis-induced secondary angle closure)

Clinical Presentation

By definition, angle closure suspects are clinically asymptomatic. A shallow anterior chamber may be a hint at a narrow anterior chamber angle with possible angle closure. On gonioscopy, two or more quadrants of appositional iridotrabecular contact are seen, but no PAS. IOP is within normal limits. No signs of GON as well as no signs of previous ▶ acute angle closure are to be found. No secondary causes for shallow anterior chamber or narrow anterior chamber angle are present.

Diagnosis

▶ Angle closure is diagnosed on gonioscopy.

By indentational gonioscopy, appositional angle closure can be confirmed, and PAS can be excluded. ▶ Ultrasound of the anterior segment may rule out other pathologies causing angle closure.

Biomicroscopy with accurate assessment of the anterior chamber as well as the posterior segment should be performed, and attention should be paid whether there are signs of previous attacks of ▶ acute angle closure.

A provocative test with mydriatics is not recommended as it provides little additional information. Even when negative, the potential for angle closure is not ruled out.

Differential Diagnosis

Previous attacks of ▶ acute angle closure, ▶ angle closure glaucoma, and narrow angle or angle closure secondary to other pathologies should be considered and ruled out.

Prophylaxis

Evidence for prophylactic treatment is ambivalent. In cases of two or more quadrants of iridotrabecular contact, prophylactic treatment may be considered. In the fellow eye of primary ▶ acute angle closure, prophylactic treatment is clearly indicated.

Angle closure suspects should be informed about the clinical signs of ▶ angle closure and advised to get immediate ophthalmic attention in case of symptoms.

Therapy

The aim of prophylactic treatment is to prevent ▶ acute angle closure as well as the development of PAS and chronic angle closure.

As angle closure suspects are asymptomatic, the risks of treatment are to be balanced against the perceived risk of progression to ▶ acute angle closure or chronic angle closure. If treatment seems indicated, a prophylactic laser ▶ iridotomy is the therapy of choice.

Prognosis

Only a small percentage of individuals with a narrow angle develop ▶ acute angle closure or ▶ angle closure glaucoma. No valid tests exist to predict which patients are likely to progress.

Epidemiology

Female gender, older age, and hyperopia are factors associated with shallower anterior chambers and may predispose for angle closure. Besides, relatives of subjects with ▶ angle closure glaucoma are at greater risk to develop ▶ angle closure, although estimates of risk vary greatly.

Cross-References

- ▶ Acute Angle Closure
- ▶ Angle Closure
- ▶ Angle-Closure Glaucoma
- ▶ Biomicroscopy, Ultrasound, of Anterior Segment
- ▶ Iridotomy
- ▶ Mydriasis Induced Secondary Angle Closure

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Aniridia, Traumatic

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Synonyms

Traumatic iris loss

Definition

Partial or total loss of iris tissue due to ocular trauma.

Etiology

Traumatic aniridia is the result in open globe injuries after extrusion of iris tissue through the wound. The loss of tissue itself is due to either direct mechanical force during the trauma or secondary due to ischemia and necrosis. Often, during primary reconstructive surgery in open globe injuries prolapsed necrotic iris tissue is removed. In rare cases of extreme blunt force trauma, a total iridodialysis may occur, even if there was no open globe injury.

Clinical Presentation

Segments of the iris or the total iris are missing giving views of the lens or posterior chamber and vitreous.

Diagnostics

If the cornea is clear, diagnosis of traumatic aniridia is straightforward. It may be difficult or impossible in cases of corneal edema, corneal scarring, hematocornea, or hyphema which are often present after severe ocular trauma. In those cases, ultrasonic examination of the anterior segment could be helpful.

Differential Diagnosis

Congenital aniridia.

Prophylaxis

Primary surgery of open globe trauma should be performed as early as possible. All manipulations (e.g., at the slit lamp) should be avoided and all exams which are not immediately necessary (e.g., CAT scans) should be postponed to prevent suprachoroidal hemorrhage with consecutive extrusion of intraocular tissue. During surgery, as much iris tissue should be preserved as possible (Kuhn 2008).

Therapy

If the patient suffers from light sensitivity, a soft iris print contact lens can be fitted. In case of partial iris loss, secondary surgery with iris sutures or artificial iris (iris prosthesis, IOL, iris ring) can improve function and cosmetics (Chung et al. 2009). In pesudophakic eyes, total or segmental aniridia implants or IOLs can be used.

Prognosis

Eyes with traumatic aniridia often have a significant comorbidity due to the trauma (damage of cornea, lens, retina, and optic nerve) which determines the outcome. Moreover, traumatic aniridia is often associated with glaucoma which may be difficult to treat.

Epidemiology

In a large retrospective series of cases of contusion and rupture of the globe, the incidence of traumatic aniridia was reported to be 1% (Viestenz and Küchle 2001).

Cross-References

- ▶ Open Globe
- ▶ Terson Syndrome Caused by Subarachnoid Hemorrhage

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Aniseikonia Correction Rule

- ▶ Knapp's Law

Anisocoria

- ▶ Anisocoria of Small Pupil: Horner Syndrome
- ▶ Anisocoria of the Small Pupil

Anisocoria of Small Pupil: Horner Syndrome

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Synonyms

Anisocoria; Horner syndrome; Miosis; Oculosympathetic paresis

Definition

Anisocoria refers to a difference in pupil size (typically > 0.4 mm) between the two eyes. Miosis refers to pupillary constriction and mydriasis to relative dilation. Horner syndrome (HS) is characterized by the clinical constellation of ipsilateral miosis, ptosis (and upside down ptosis), and variable facial or body anhidrosis resulting from oculosympathetic paresis (i.e., damage to the sympathetic nervous system supplying the pupil and eyelid).

Etiology

Causes of anisocoria resulting from an abnormally small pupil include:

I. Ocular disease
   1. Anterior uveitis (i.e., posterior synechiae)
   2. Prior ocular surgery (e.g., iris damage)
   3. Pseudoexfoliation syndrome
II. Pharmacologic miosis (e.g., pilocarpine eye drops or other miotics)
III. Horner syndrome (HS)
   1. First order
   2. Second order
   3. Third order

The ocular sympathetic pathway is a three-neuron arc. The first-order neurons lie in the ipsilateral posterolateral hypothalamus. Their axons travel ipsilaterally in the lateral tegmentum of the midbrain, pons, and medulla to the ciliospinal center of Budge in the intermediolateral cell column in the spinal cord at the C8, T1, and T2 levels. The second-order axons of the preganglionic neurons then exit via the dorsal roots at T1 and travel in the cervical sympathetic chain. This path brings them near the apical lung and the subclavian artery. They ascend in the sympathetic chain to synapse with the third-order postganglionic neurons in the superior cervical ganglion near the bifurcation of the carotid artery at C3–C4. The pupillary postganglionic fibers travel along the internal carotid artery while the vasomotor and sudomotor fibers follow the external carotid artery. After entering the cavernous sinus with the internal carotid, the pupillary postganglionic fibers join the abducens nerve for a short course and then enter the orbit with the ophthalmic branch of the trigeminal nerve. Running in the long ciliary nerves, these fibers innervate the iris dilator and Müller muscle of the superior lid.

The first-order neuron can be damaged by compression (e.g., tumors of the hypothalamus, skull base or spinal cord, Chiari malformation), ischemic disease (e.g., lateral medullary syndrome), and other central nervous system (CNS) diseases (e.g., infection, inflammation, infiltration, toxin, demyelinating disease, or trauma). The second-order neuron can be compressed as it travels over the lung apex by a neoplasm (e.g., Pancoast tumor of the lung), central venous catheterization, traumatic or surgical dissection of the neck, aortic aneurysm, a cervical rib, and birth trauma (e.g., brachial plexus injury). In infants and children, a neuroblastoma of the sympathetic chain or any compressive lesion in the neck or upper chest can lead to HS. Possible damage to the third-order neuron includes dissection of the carotid artery (spontaneously or related to trauma), carotid-cavernous fistula, cluster or migraine headache, and mass lesions causing damage at the cavernous sinus or posterior orbit.

Clinical Presentation

HS presents with anisocoria and an ipsilateral miotic pupil, mild (less than 1–2 mm) ptosis, upside down ptosis (lower lid retractor), and possible facial or hemibody anhidrosis depending on the site of the lesion. The anisocoria in HS is more notable in darkness. In addition, there is typically a lag in the dilation of the involved pupil in HS (i.e., dilation lag) that can be detected by observing the anisocoria in the dark for 5–10 s and demonstrating a greater anisocoria initially that improves over time. Other evidence of sympathetic denervation such as ptosis from loss of input to Müller muscle is typically present but may be absent in a significant minority of cases or might be masked by contralateral dermatochalasis. Other associated clinical "neighborhood signs" can help define the likely location of the lesion. Lateral medullary stroke (i.e., Wallenberg syndrome) often features HS with variable combinations of ipsilateral facial sensory loss, contralateral hemibody pain, and temperature loss, dysphagia, dysarthria, nystagmus, vertigo, ataxia, palatal myoclonus, and hiccoughs. Other patterns of weakness and sensory loss as well as cranial nerve deficits can point to lesions in the brainstem or spinal cord. An acute onset with neck pain can accompany a cervical dissection

of a carotid or vertebral artery, especially with stroke or transient ischemic attack symptoms. Involvement of the abducens nerve, potentially together with involvement of the oculomotor and trochlear nerves, can suggest a cavernous sinus or superior orbital fissure localization.

Diagnostics

A careful and complete history is necessary to firmly establish the time course of presentation as well as accompanying symptoms in the HS. One can often use old photographs, such as a driver's license or identification card, to determine whether deficits are longstanding or not.

Examining the pupils both in light and dark conditions to identify the abnormal side is the first step. More pronounced anisocoria in darkness indicates that miotic pupil has failed to dilate appropriately, and this finding suggests a HS lesion to that side.

Pharmacologic confirmation of HS is classically made by instillation of 2–4% cocaine eye drops into both eyes. Cocaine inhibits reuptake of norepinephrine at the junction. Dilation of the pupil is the normal physiological response to the accumulation of norepinephrine. An anisocoria of greater than 0.8 mm 30 min following instillation is highly suggestive of an HS. However, cocaine drops are difficult to obtain and require compliance with institutional and state regulations for controlled substances. After a positive cocaine test, instillation of 1% hydroxyamphetamine (Paredrine test) can localize the HS to a preganglionic or postganglionic lesion. This Paredrine test should be performed at least 24–48 h after the cocaine test. Hydroxyamphetamine promotes release of norepinephrine from the third-order neuron. Dilation of the pupil and resolution of the anisocoria after a positive prior cocaine test for HS confirms the integrity of the third-order fibers and indicates a first- or second-order lesion HS. Alternatively, topical apraclonidine can be used to diagnose an HS and is more readily available than topical cocaine or hydroxyamphetamine. Under normal conditions, it acts as a weak alpha-1 and a stronger alpha-2 adrenergic agonist. In a normal pupil, the alpha-2 effect dominates, and the pupil either does not react or at most constricts mildly. However, denervation of the iris dilator results in supersensitivity of the alpha-1 receptors which are upregulated. Thus, instillation of 0.5–1% apraclonidine results in mydriasis of the smaller pupil and often a reversal of the ptosis in HS. However, this supersensitivity may take up to 1 week to develop following sympathetic denervation, and if the patients clearly have an HS clinically, then imaging the sympathetic axis without topical testing might be indicated.

When the presentation is acute, head CT is mandatory to evaluate for stroke, particularly hemorrhage, and a concomitant head and neck CT and CT angiography (CTA) provides a rapid means of evaluation for arterial dissection that can be performed during the same session. The ordering physician must remember that both carotid and vertebral dissections typically occur in the neck and include the neck in the studies. Cerebral angiography, however, remains the gold standard for diagnosis of arterial dissection when CT angiography is not conclusive. In the nonurgent setting, MRI and MR angiography (MRA) of the head and neck (down to T2 in the chest) is probably a superior initial study for an unexplained HS. As noted above, in children and infants, neuroblastoma of the sympathetic chain is a concern. Imaging of the entire ocular sympathetic axis can be combined with laboratory evaluation of urine and/or blood for elevated catecholamines (e.g., homovanillic acid and vanillylmandelic acid).

Differential Diagnosis

1. Anisocoria with a large pupil
2. Adie pupil
3. Physiologic anisocoria
4. Third nerve palsy
5. Adhesions of the iris

6. Phamacologic mydriasis
7. Pharmacologic miosis

Prophylaxis

Not applicable

Therapy

Treatment should be directed toward the underlying etiology. The ptosis of HS may be treated surgically once the etiology is confirmed and treated.

Prognosis

The prognosis for Horner syndrome depends on its etiology.

Cross-References

- ▶ Anisocoria: Big Pupil
- ▶ Proptosis

Further Reading

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Anisocoria of the Small Pupil

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5. Adhesions of the iris

6. Phamacologic mydriasis
7. Pharmacologic miosis

Prophylaxis

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Therapy

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Prognosis

The prognosis for Horner syndrome depends on its etiology.

Cross-References

► Anisocoria: Big Pupil
► Proptosis

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Anisocoria: Big Pupil

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Synonyms

Adie syndrome; Adie's tonic pupil; Holmes-Adie syndrome; Little old Adie's pupil

Definition

The Adie tonic pupil (ATP) is characterized acutely by a dilated ipsilateral pupil with an impaired light reaction. Over time the pupil becomes smaller (i.e., "little old Adie") and develops a tonic near reaction (light-near dissociation). ATP is caused by damage to the parasympathetic innervation to the eye at the level of the ciliary ganglion or postganglionic fibers.

Etiology

ATP is caused by damage to the parasympathetic innervation to the iris and ciliary body at the

ciliary ganglion or postganglionic nerves. Initially, the pupil reacts poorly to both light and accommodation and thus can mimic a pharmacologically dilated pupil. Over the next few days to weeks after the acute denervation, however, postganglionic axons can regenerate, but some regeneration may occur aberrantly. Normally, there are up to 30 times more parasympathetic axons arising from the ciliary ganglion and destined for the ciliary body compared with the pupil. Thus, during aberrant regeneration, axons may accidentally reroute to the pupil rather than to their original destination in the ciliary body. The final result clinically is that the ATP may respond poorly to light but has a stronger and tonic reaction to accommodation (i.e., light-near dissociation). Although most cases of tonic pupils are idiopathic ATP, some tonic pupils are the result of inflammation, infection, or trauma (including surgical trauma) affecting the ciliary ganglion or postganglionic nerves. ATP is typically unilateral at onset, but up to 20% of cases become bilateral over time, and in one study, the annual rate bilateral involvement was 4%.

Clinical Presentation

The anisocoria of ATP is often discovered incidentally on routine exam or the pupil assymmetry may be noticed by the patient when looking in the mirror. Other times it is discovered by a friend or a family member of the patient. When symptomatic, there may be mild photophobia or difficulty reading (accommodation). ATP is usually painless, although some patients may complain of asthenopia (e.g., eye strain, "cramping sensation" in the affected eye secondary to spasm of the ciliary body ("ciliary cramps") or other reading difficulty). On exam, the affected pupil in the acute setting is larger, and the anisocoria is greater in the light. Over time the ATP develops the light-near dissociation, and slow re-dilation after constriction or after accomodation (i.e., "tonic" response). Tonic accommodation may also be present and can be described by patients as difficulty when changing fixation from a near to a distance visual target. Corneal sensation has been reported to be mildly depressed in some patients. On slit lamp examination, the pupil may be irregular, exhibiting sector or diffuse paresis or vermiform movements in the intact iris segments. In contrast to the third nerve palsy with pupil involvement, there should be no evidence for ptosis or extraocular motility deficit in ATP alone. The iris should be examined carefully for evidence of iris atrophy, synechiae, or sphincter tear that would suggest alternative diagnoses for the anisocoria.

Diagnostics

The distinguishing clinical features of ATP have been noted above. If decreased deep tendon reflexes are also present, ATP would then be a component of the full Holmes-Adie syndrome. Examining old photographs can help distinguish whether the anisocoria is old or new and the presence of a photographically documented and long standing ATP can often obviate the need for further testing. If the typical features of ATP are present and the findings are neurologically isolated then pharmacological testing is generally not necessary. However, in some cases there remains clinical uncertainty and in this setting, dilute 0.1% pilocarpine can be helpful in differentiating ATP from other etiologies of anisocoria. In ATP, cholinergic denervation supersensitivity leads to more constriction to dilute pilocarpine in comparison to the normal eye. This finding would support the diagnosis of ATP over iris sphincter abnormality, an atonic pupil (no iris tone), or pharmacologic mydriasis. The ATP can be distinguished from the pupil involved third nerve palsy by the absence of ptosis or motility deficit and the sector nature of the iris paresis. It should be kept in mind that only 80% of patients with ATP demonstrate cholinergic supersensitivity (false negative) and that this same supersensitivity reaction can also be noted in patients with CN III preganglionic lesions (false positive). The dilute topical pilocarpine should be applied to both eyes, as some patients, particularly those with normal but lightly pigmented irises, may respond to dilute pilocarpine. In addition, the fellow eye serves as a control to insure that the pilocarpine is

working and that it is not inadvertently undiluted (e.g., 1% pilocarpine).

Differential Diagnosis

ATP produces anisocoria that is typically worse in the light compared with the dark. The differential diagnosis of anisocoria greater in the light includes pharmacologic mydriasis, iris abnormality (e.g., iris atrophy, synechiae, atonic pupils, surgical trauma), or third nerve palsy with pupil involvement.

Tonic pupils can occur after local orbital syndromes (e.g., infection, inflammation, neoplasm, trauma, orbital surgery) and in systemic autonomic neuropathies (e.g., Charcot-Marie-Tooth disease and Guillain-Barre Syndrome). Local anesthesia due to an inferior dental block or retrobulbar blocks or alcohol injection can produce a tonic pupil. Other less common causes of a tonic pupil include ischemia, toxicity (e.g., quinine and trichloroethylene), and as a paraneoplastic syndrome. Although ATP can be associated with decreased deep tendon reflexes (i.e., Holmes-Adie syndrome), typically ATP is otherwise neurologically isolated. In contrast, patients with ATP and other autonomic cardiac, sweating, or gastrointestinal symptoms or signs should be considered for further neurologic and systemic testing for diffuse dysautonomia (i.e., Ross syndrome).

Although the Argyll Robertson pupil (miotic pinpoint pupils with bilateral light-near dissociation) is classically described in syphilis, bilateral tonic pupils similar to ATP can also occur in syphilis. We recommend consideration for syphilis testing in non-isolated ATP or in bilateral cases of ATP. Although imaging is not typically needed for typical ATP, atypical cases or unexplained bilateral light-near dissociation (especially without the tonic near reaction) of the pupils might still need imaging (e.g., cranial MRI) directed at the dorsal midbrain.

Therapy

The majority of patients are asymptomatic and do not require treatment beyond simple reassurance of the benign nature of the finding. Some patients, however, may complain of reading difficulty secondary to accommodation paresis in the early denervation stage. Although this symptom usually resolves over time, asymmetric bifocal glasses (unilateral frosted or unequal power) may help improve reading while reinnervation occurs. Application of low-dose topical pilocarpine may also ease symptoms of anisocoria. A few of our patients have used PRN dosing of low-dose topical pilocarpine for cosmetic reasons and social occasions. However, this pharmacologic intervention may also induce ciliary spasm and myopia and should therefore be used with caution.

Prognosis

The majority of ATP are benign and only require reassurance and supportive care. Ross syndrome, however, should be referred for systemic and neurologic evaluation. Patients with positive syphilis serology should be treated with penicillin and undergo neurologic evaluation and cerebrospinal fluid evaluation.

Epidemiology

ATP occurs in about 0.2% of the population (2/1000 individuals). It is more common in females with a 2.6/1 ratio, and it has been found to appear in all ages.

Cross-References

- ▶ Anisocoria
- ▶ Adie's Tonic Pupil

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Annular Tendon

► Annulus of Zinn

Annulus of Zinn

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Synonyms

Annular tendon; Circle of Zinn-Haller; Common tendinous ring

Definition

The annulus of Zinn is a dense, fibrous ring of connective tissue located at the apex of the orbit that is the origin of four of the six extraocular muscles – the superior rectus, inferior rectus, lateral rectus, and medial rectus. In addition to its relation to the extraocular muscles, the annulus of Zinn has important connections with some of the cranial nerves. The optic, oculomotor, and abducens nerves all pass through the annulus of Zinn, while the trochlear nerve travels just medial to the annulus of Zinn. The nasociliary nerve is the sole portion of the ophthalmic division of cranial nerve V which passes through the annulus of Zinn. Finally, the medial portion of the annulus of Zinn is fused to the optic nerve sheath. This may be the reason that there is pain during eye movements for individuals experiencing optic neuritis.

Cross-References

► Optic Neuritis

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Anomalous Trichromats

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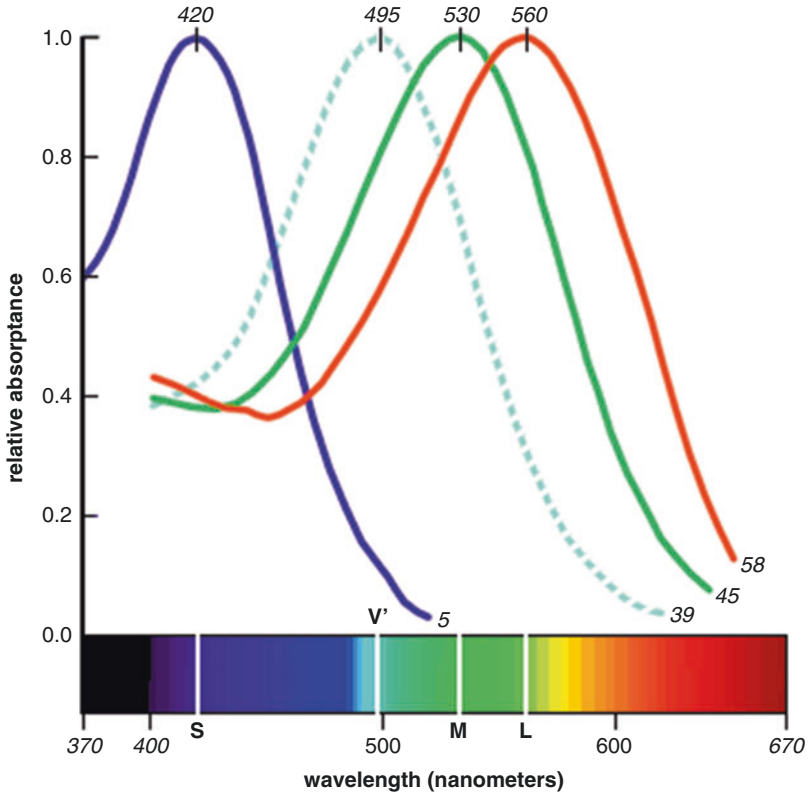
Synonyms

Color "blindness"; Color vision deficiency

Definition

Anomalous trichromacy (a type of color vision deficiency) is an alteration in the spectral sensitivity of one of the three cone cell receptors in the retina



Anomalous Trichromats, Fig. 1 Human cone absortion cuves (normalized to equal peak absorptance (1.0) on a linear vertical scale; wavelength of peak absorptance in italics, number of photoreceptors measured for each curve at base of curve (Data from Dartnall et al. 1983; Bowmaker and Mollon 1983). (Bruce MacEvoy 2009)

that make up the color spectrum (Fig. 1) (Dartnall et al. 1983; ebook: Color blind essentials 2016).

Etiology

In the nineteenth century, Thomas Young and Hermann von Helmholtz theorized that human color vision is composed of a combination of three colors "trichromatic" (red, blue, and green). Color perception in the human eye is attributed to three different types of cone photoreceptor (opsin) cells. Gunner Svaetichin (1956) proved the existence of these cells and their sensitivity to different wavelength ranges (Svaetichin 1956). They contain a specific photopigment, which is most sensitive to a specific spectrum of light. The brain combines input from all the three cell types to interpret color. S-cones are sensitive to short wavelengths with normal peak absorption at approximately 420 nm (blue [tritan] light receptors). M-cones are sensitive to medium wavelengths and normally peak at about 540 nm (green [deutan] light receptors). L cones are sensitive to long-wavelength light and their normal peak is at about 560 nm (red [protan] light receptors). Anomalous trichromats have three types of cones, but one of the three types has a spectral sensitivity shifted from the normal cones (Sharpe and Gegenfurtner 2001; ebook: Color blind essentials 2016).

Nathan et al. (1986) isolated the genes encoding the S, M, and L-cone opsins (Nathan et al. 1986). Long-wavelength (L) and middle-wavelength (M) genes share over 98% nucleotide identity and are found on the X-chromosome at Xq28 (genetic designation OPN1LW and OPN1MW, respectively) with a normal variability in the number of these genes per chromosome. The gene for the short-wavelength (S) cone opsin shares only about 40% nucleotide similarity with the other opsin genes. It is found on chromosome 7 at 7q32 (OPN1SW) (Parker and Parker 2007).

Genetic causes of anomalous trichromacy are due to inherited mutations in these genes. Red and green visual anomalies (L and M opsins) are most common and are X-linked recessive. The L and M genes are adjacent to each other on the X-chromosome and as they are nearly identical, misalignment of these genes can occur between parent chromosomes leading to recombinant crossovers between the two genes. Protanomaly makes the L-cone more like the M-cone and deuteranomaly makes the M-cone more like the L-cone. With the absorption maxima of the cones shifting closer together, the ability to discern reds and greens decreases. Defects in the blue opsin (S) are inherited in an autosomal-dominant fashion and cause difficulty in distinguishing the blue-yellow spectrum, which is known as tritanomaly (Parker and Parker 2007).

Acquired causes of color vision deficiency are due to damage along the conducting paths of the optical system. Type 1 (red-green) mimics protanomaly due to more efficient short-wavelength processing and is associated with progressive cone dystrophy and retinal pigment epithelium dystrophies. Type 2 (red-green) resembles deuteranomaly but with a greater reduction in short-wavelength sensitivity and is associated with optic neuritis. Type 3a tritan type with increased efficiency to short wavelengths is found in central serous chorioretinopathy and age-related macular degeneration. Type 3b tritanomaly is found in rod and rod-cone dystrophies, retinal vascular disorders, peripheral retinal lesions, glaucoma, and autosomal-dominant optic atrophy (Birch 2001). Drugs including digoxin, ethambutol, chloroquine, hydroxychloroquine, phenytoin, and sildenafil can also cause color vision deficits as well as toxins such as lead, alcohol, and tobacco.

Clinical Presentation

Anomalous trichromacy presents as a smaller color spectrum.

Protanomaly presents as "red weakness" in terms of color power (saturation/depth of color) and brightness and red is perceived as much darker.

Deuteranomaly presents as "green weakness."

In both protanomaly and deuteranomaly, the main axis of colors of confusion is the same: red, orange, yellow green, and brown. However, the colors of the confusion for blue-purple hues are perceived very differently between the groups. Protanomaly defects may see violet shades as blue as the red component is weakened (colorvisiontesting.com).

Tritanomaly presents as a difficulty in distinguishing between yellow and blue.

Diagnosis

There is a range of color blindness tests in diagnosis of color vision deficiency. Seebeck developed color matching without the use of color naming in 1837 in which sample color was matched to more than 300 colored papers. This was the basis for the Holmgren wool test (1877) in which skeins of colored wool are matched (ebook: Color blind essentials 2016).

Modern color vision deficiency testing:

- **Anomaloscope**: This is based on the Rayleigh match in which a mixture of red and green light sources has to be matched with a yellow light source. It is probably the most precise commercially available diagnostic test. This enables discovery of red-green color deficiency. Some anomaloscopes also include the Moreland match (blue-green), which tests for tritan defects. People with protan defects use more red as opposed to deuteranomaly where more green is used for matching.

The International Commission on Illumination defined a color space chromaticity diagram in 1931(CIE31), which is the basis for many of the currently employed color vision tests. A graph was compiled based on subjects matching a test light color source to three adjustable light sources

(red, green, and blue). Confusion lines defined the colors that were hard to differentiate by color-blind people, with the copunctal points being where they converged (Smith and Guild 1931–32; CIE 1932).

- **Pseudoisochromatic plates**: The first published plates were by J. Spelling, which were a predecessor to the most famous type of color-blind test plates, the Ishihara plate test (Ishihara 1917). Patterns of differently colored dots, which correspond to colors of confusion, are used to differentiate color deficiencies. Types of plates include vanishing design where only people with good color vision can see the design, transformation design where color-blind people see a different sign to normal color vision, and hidden digit design where only color-blind people see the design and classification design which differentiates deutan from protan defects. Ishihara plates only differentiate red-green vision deficiencies. The 24 HRR (Hardy et al. 1954) plates also include tritan defects (Hardy et al. 1954).
- **Arrangement tests**: These also are base on copunctal points and dynamic test-colored disks or plates have to be arranged in the correct order. These tests include the Farnsworth D-15 arrangement test, Farnsworth-Munsell 100 hue test, and Lanthony desaturated D-15 test.
- **Lanterns**: These are most often used as vocational tests and were introduced by railway companies to establish whether employees could distinguish signals. These include Holmes-Wright, Farnsworth (Falant), Beyne lantern, Giles-Archer, and Eldridge-Green lanterns.
- **Computer-based testing**:
- **Genetic testing** (in parallel to physical testing).

Differential Diagnosis

- Dichromacy (one cone type missing)
- Monochromacy (two cone types missing)
- Complete achromatopsia (rod "monochromacy") – all cone types missing
- Cerebral achromatopsia/dyschromatopsia
- Disorders of the ocular media
- Macular detachment
- Cone dystrophies/degeneration
- Macular dystrophies/degeneration
- Vascular and hematologic diseases
- Glaucoma and optic nerve disease (e.g., autosomal-dominant optic atrophy)
- Diseases of the central nervous system (e.g., multiple sclerosis) and other organs (e.g., diabetes mellitus)
- Toxic agents and drugs (see list under "Etiology")

Prophylaxis

There is currently no prophylaxis for anomalous trichromacy. With improving genetic testing, identification of mutated genes may be possible.

Therapy

There is presently no cure for color-blind people. Neitz et al. have shown genetic therapy with subretinal injection of the missing genes in monkeys to improve color vision (Neitz and Neitz 2011).

Colored filters (lenses, glasses, or tools such as the Seekey) are available and are used over one eye to improve distinguishing between colors. There is also a range of computer-based tools available in aiding color-deficient people.

If the cause of color deficiency is acquired, then the underlying disease should be targeted appropriately or the offending drug/toxic agent removed.

Prognosis

Hereditary abnormal trichromacy is a stable condition.

Epidemiology

Color vision deficiency is a very common condition affecting approximately 8% of men and 0.5% of women. It is most common in people of European descent. Deuteranomaly is the most common affecting 4.63% men and 0.36% females. Protanomaly affects 1.08% males and 0.03% females (male predominance due to x-linked recessive inheritance). Tritanomaly is autosomal dominant and so is found equally in men and women (ebook: Color blind essentials 2016).

Cross-References

► Cone Dystrophies/Degeneration

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Anophthalmic Socket

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Definition

The absence of the globe and ocular tissue from the orbit.

Etiology

The majority of cases of anophthalmos are seen following evisceration or enucleation. Congenital anophthalmos is rare and due to the arrest of embryogenesis during formation of the optic vesicle. A genetic, infectious, or toxic etiology may be identified. Recent studies point to the role of SOX2 haploinsufficiency, as this variant was found in up to 10% of patients with anophthalmos or severe microphthalmia.

Clinical Presentation

Disfigurement may result from the volume deficit. An orbital implant is typically placed at the time of evisceration or enucleation. An ocular prosthesis is fitted subsequently. In the absence of an implant (or with placement of an undersized implant), postenucleation/evisceration socket syndrome (PESS) may result, manifest as enophthalmos, deep upper eyelid sulcus, ptosis,

lower lid laxity, ectropion or entropion, and shallowing of the inferior fornix.

Differential Diagnosis

Microphthalmos

Therapy

Eyelid Malposition

The volume deficit should first be corrected with an orbital implant (if none present) or an orbital floor implant (if an undersized intraconal implant is present). Depending on the degree of residual lower lid laxity and involvement of the medial or lateral canthus, a lateral tarsal strip or fascial sling is usually sufficient. Upper lid ptosis may then be addressed.

Socket Contracture

The socket is particularly susceptible following trauma, recurrent inflammation due to an inadequate prosthesis, or radiotherapy. Please refer to the entry on *Socket Contracture* for more information on this topic.

Orbital Implants

The goal of the implant is to replace the volume deficit, maximize motility, provide comfort, be aesthetically acceptable, and cause few complications. Numerous options are available, but there is no consensus regarding the ideal implant. The surgeon must first select the appropriate size and then consider whether the implant should be porous or nonporous, spherical or nonspherical, wrapped or unwrapped, and directly or indirectly coupled. Extraocular muscles were previously sutured over the implant but are now more commonly sutured directly to the implant itself or its overlying wrapping material. Tenon's capsule and conjunctiva are closed over the amalgam. A conformer is placed until an ocular prosthesis can be fit. Please refer to the entry on *Orbital Implants* for further information on this topic.

Congenital Anophthalmos

Treatment is directed toward the first stimulating growth of the orbit and adnexal soft tissues and then providing orbital volume replacement and soft tissue reconstruction. Progressively larger acrylic conformers are used to expand the socket. Spherical orbital implants, dermis fat grafts, and other socket/orbital expanders are then used for reconstruction. More recently, the use of injectable self-inflating hydrogel expanders has been proposed as a safer, less-invasive alternative in orbital reconstructive surgery.

If unilateral, ensuring the health and protection of the seeing eye with routine examinations is imperative. If bilateral, psychosocial support and early interaction with the appropriate agencies is essential in optimizing development, genetic counseling may be helpful in assessing the potential risk in future children.

Practice Patterns

Su and Yen (2004) surveyed members of the American Society of Ophthalmic Plastic and Reconstructive Surgery (ASOPRS) regarding their practice patterns after enucleation and evisceration. The porous polyethylene implant was used most frequently after both enucleation (42.7%) and evisceration (42.3%), followed by the porous hydroxyapatite implant (27.3 and 25.9%) and nonporous implants (19.9 and 25.7%). The majority of surgeons (59.8%) do not to wrap their implants. For those who do, human donor sclera was most commonly used (25.2%), followed by polyglycolic acid mesh (7.2%). Implant pegs were used in only 8.1% of cases. The most common complications included pyogenic granuloma (13.7%), exposure (5.7%), and discharge (5.7%).

Cross-References

- ▶ Contracted Socket
- ▶ Implants, Orbital
- ▶ Nanophthalmos

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Anterior Basement Membrane Dystrophy

► Map-Dot-Fingerprint Dystrophy (Epithelial/Anterior Membrane Dystrophy)

Anterior Capsule

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Definition

The anterior capsule is the anterior part of the membranous structure which envelopes the crystalline lens (lens capsule).

Anatomy

The lens capsule encloses the lens material (lens fibers). With a thickness of 3–5 µm at the posterior pole, 5 µm at the anterior pole, 11 µm at the lens equator, and 25–30 µm in the anterior mid-periphery, it is the thickest basement membrane of the body and consists mainly of collagen type IV.

Importance for Cataract Surgery

In extracapsular cataract surgery techniques such as phacoemulsification, the anterior capsule needs to be opened to allow for extraction or emulsification/aspiration of lens material and subsequent implantation of an artificial intraocular lens. While there are different methods for opening the capsule, the most preferable way is the continuous curvilinear capsulorrhexis (CCC) which minimizes the risk of radial tears in the lens capsule.

The inside of the anterior capsule is sometimes polished during cataract surgery to remove lens epithelium and lower the incidence of capsular fibrosis.

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Anterior Capsule Opacification (ACO)

► Capsular Bag Opacification

Anterior Capsulorhexis

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Synonyms

Capsulorrhexis; Continuous curvilinear capsulorhexis (CCC)

Definition

The capsulorhexis (greek rhexis: to break) is a technique of anterior capsulotomy. The capsulorhexis delineates a circular and continuous central opening in the anterior capsule. It allows expression or phacoemulsification of the lens nucleus. Today, the continuous curvilinear capsulorhexis (CCC) is the standard technique for the surgical approach to the anterior capsule.

This method allows an in-the-bag phacoemulsification and in-the-bag intraocular lens implantation.

Advantages of this method are a lower risk of radial tears and vitreous loss. In addition, by using this approach the capsule can be stretched by 60%.

Other anterior capsulotomy techniques with a radial discontinuity (envelope capsulotomy, can-opener technique) increase the risk of radial tears with vitreous loss.

Epidemiology

See ▶ Cataract Surgery article.

History

The idea dates back to Neuhann, Gimbel, and Shimizu. In the mid 1980s, Neuhann (capsulorhexis) and Gimbel (continuous tear capsulotomy) first described the capsulorhexis technique independently as a principle controlling continuous tearing. Shimizu defined the surgical approach as circular capsulotomy.

The outcome of these scientific achievements is today's commonly used definition of a continuous circular capsulorhexis (CCC).

Clinical Features

Conducting instruments are either a cystotome or a bended needle.

Tests

Important to ascertain an indication for cataract surgery are an efficient ophthalmological examination and a detailed anamnesis (any amblyopia, other eyes diseases, precedent eye surgeries, pharmaceutical anamnesis, and symptoms of cataract). An effective capsulorhexis is at risk by loose zonular fibers.

Differential Diagnosis

The technique of opening the anterior capsule is chosen according to operation technique.

Further capsular opening methods in the following are:

- Vitrectorhexis (vitrector-cut anterior capsulectomy)
- Can-opener technique (letter box – technique)
- Minicapsulorhexis or Two stage capsulorhexis
- Linear capsulotomy
- Capsulopuncture
- Posterior capsulorhexis, capsulotomy
- Capsulorhexis shape and size
- Fugo blade
- High Radiofrequency diathermy capsulotomy

Etiology

See "History" section above.

Treatment

The capsulorhexis should be practiced continuously, central and arched. It consists of two characteristical movements: shearing and ripping. The conducting instruments are either a cystotome or a bended needle.

Before starting to perform the capsulorhexis, a rocking test with a tip or 27- or 30-gauge cannula should be performed to evaluate lens stability.

While performing the capsulorhexis, the anterior chamber has to be deep. Either inserting of viscoelastic agent in the anterior chamber or an irrigation from an anterior chamber maintainer is possible.

After that the magnification of the microscope enhances the view of the anterior capsule with working in a dark setting and a focal light on the surgical table. The stabilization of the glob is given by grasping the paracentesis site or the limbus. The initial tear in the anterior capsule is performed centrally. Now an instrument

(cystotome or bended needle) is introduced through a paracentesis. By connecting these instruments with a syringe, the viscoelastic agent or BSS can be inserted.

Hereafter, the anterior capsule is punctured by the needle which is swept afterwards drawing a curvilinear (center – laterally – circumferentially). The created capsular flap is dragged from the forceps 45° to the limbus. The capsulorhexis is triggered by shearing. The flap is flipped and pulled in the direction of the required rhexis (parallel to the limbus).

Cross-References

- ▶ Aspiration Curette
- ▶ Can-Opener Technique
- ▶ Capsulotomy
- ▶ Cataract Surgery
- ▶ Posterior Capsulorhexis

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Anterior Capsulotomy Techniques

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Definition

Anterior capsulotomy techniques are various methods for opening the anterior capsule. The major performed technique is the manual continuous curvilinear capsulorhexis for preparing the phacoemulsification surgery. Other methods include the vitrectorhexis capsulotomy, the multipuncture can opener technique, the radiofrequency diathermy, and the plasma blade capsulotomy, mainly performed in pediatric cataract surgery.

Indication

The indication is given in the severity of cataract, age of the patient, and special anatomical features.

Contraindication

There are the general contraindications for the phacoemulsification and the extracapsular cataract surgery technique.

Techniques and Principles

Depending on the method, different instruments are needed. In the following, the cystotome, the capsulorhexis forceps, the aspiration handpiece, the vitrector, and the Fugo plasma blade tip are to be mentioned.

For details of the method, it is referred to especially written articles.

Outcome

Because of today's performed advanced and sensitive methods of anterior capsulotomy techniques, the outcome is very well after a complication-free intervention.

Complications

Serious complications are rare. There are the general risks of the cataract surgery like inflammation, bleeding, retinal detachment, increase or decrease of intraocular pressure, corneal opacity, iris damage, radial tears, vitreous loss, Irvine-Gass syndrome, surgical-induced astigmatism (SIA), and over- or under-correction or temporary double vision.

History

Reference is made to the respective techniques.

Clinical Features

Depending on the method, different instruments are needed. In the following, the vitrector, the cystotome, the capsulorhexis forceps, the aspiration handpiece, and the Fugo plasma blade tip are to be mentioned.

For details, it is referred to especially written articles.

Cross-References

- ▶ Anterior Capsulorhexis
- ▶ Anterior Segment Surgery
- ▶ Aspiration Curette
- ▶ Can-Opener Technique
- ▶ Cataract Surgery

Further Reading

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Anterior CCC Optic Capture

- ▶ Anterior Optic Capture

Anterior Chamber

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Definition

The anterior chamber of the eye is the space between the posterior surface of the cornea and the anterior surface of the iris and lens which is filled with aqueous humor.

Anatomy

The anterior chamber is limited anteriorly by the cornea and posteriorly by the iris and the pupil. The anterior chamber angle at the junction between cornea and iris consists of the following structures:

Schwalbe's line
Canal of Schlemm and trabecular meshwork
Scleral spur
Anterior surface of the ciliary body
Iris

The depth of the anterior chamber can vary between individuals. It is deeper in myopia, aphakia, and pseudophakia. In the adult emmetropic eye it has a central depth of about 3 mm. It is most shallow just centrally of the angle. The anterior chamber volume in the emmetropic eye is approximately 250 µl.

Aqueous Flow

The anterior chamber is filled with aqueous humor which is produced by the ciliary epithelium in the posterior chamber. The aqueous humor flows though the pupil and is drained through the trabecular meshwork and the canal of Schlemm. In a small part, it is drained via the ciliary body into the supraciliary space (uveoscleral flow). The volume of drainage of aqueous from the anterior chamber can be measured using the washout of fluorescein. The average flow rate of aqueous humor through the anterior chamber is 2.1–3.1 µl/min and varies with age and time of day. The aqueous humor in the anterior chamber is exchanged about 15 times per day.

References

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Anterior Chamber Cleavage Syndrome

▶ Axenfeld-Rieger Syndrome; Mesodermal Dysgenesis; Leukomas

Anterior Chamber Dysgenesis

▶ Microphthalmos (Microphthalmia), Anterior

Anterior Chiasmal Syndrome

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Synonyms

Junctional scotoma

Definition

In an anterior chiasmal syndrome, also known as junctional visual field loss, the junction of the anterior portion of the optic chiasm and the optic nerve is involved by disease. This condition classically manifests as a loss of central vision in the ipsilateral eye and a loss of superior temporal vision in the contralateral eye (from inferonasal crossing fibers at the optic chiasm). In the past this was attributed to involvement of a "knee" of inferonasal fibers traveling for a short course in the contralateral optic nerve (i.e., the Willebrand knee). Later work has called in to question the anatomic existence of the Willebrand knee, but it does not matter clinically because the localizing significance of the contralateral superior visual field defect (i.e., the junctional scotoma) is not diminished by the anatomic existence or lack thereof for the knee per se. In the early manifestations of anterior chiasmal syndrome, the optic discs may appear normal, even if there are significant visual changes present. However, over time, the optic discs show atrophy. Common causes of this syndrome include pituitary adenoma, parasellar meningioma, craniopharyngioma, and vascular causes, such as aneurysm of the parasellar region of the internal carotid. Alternatively, another form of anterior chiasmal syndrome-related junctional visual field loss is a monocular hemianopic visual field loss from involvement of the crossing nasal fibers (producing a monocular temporal hemianopic visual field defect) or uncrossed temporal fibers (producing a monocular nasal hemianopic visual field defect). In order to differentiate this finding of a monocular hemianopic junctional visual field defect from the junctional scotoma (superotemporal contralateral visual field defect), this type of anterior chiasmal loss is called the junctional scotoma of Traquair.

Cross-References

▶ Adenoma of the Clear Cell Type
▶ Aneurysms
▶ Craniopharyngiomas
▶ Parasellar Lesions

Further Reading

Karanjia N, Jacobson DM (1999) Compression of the prechiasmatic optic nerve produces a junctional scotoma. Am J Ophthalmol 128(2):256–258

Anterior Communicating Artery

► Communicating Arteries Anterior

Anterior Corneal Dystrophies

► Epithelial Dystrophies

Anterior Corneal Dystrophy

► Corneal Dystrophies

Anterior Cranial Fossa

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Definition

The anterior cranial fossa contains the frontal lobes of the brain, is located superior to the nasal cavity and orbits, and is one of three divisions of the floor of the cranial cavity. It is composed of portions of the frontal, ethmoid, and sphenoid bones. The anterior and lateral portions of the floor of the anterior cranial fossa are from the frontal bone, the midline portion is from the ethmoid bone, and the posterior aspect is from the body and lesser wing of the sphenoid bone. The ethmoid sinuses lie inferior to the anterior cranial fossa and are toward the midline. The posterior portion of the frontal sinuses borders the front of the anterior cranial fossa and may be used as a surgical entry point into it.

The anterior section of the anterior cranial fossa contains an attachment point for the falx cerebri known as the frontal crest. Posterior to the frontal crest is the foramen cecum, through which emissary veins connect the nasal cavity and the superior sagittal sinus. Slightly posterior to the foramen cecum lies the crista galli, a part of the ethmoid bone that is another attachment point for the falx cerebri. On either side of the crista galli lies the cribriform plate, through which olfactory nerve fibers pass through. The cribriform plate is a very thin portion of the ethmoid bone, and this unique property may be utilized when attempting to gain transethmoidal access to the brain. Lateral to the cribriform plate on either side is the orbital part of the frontal bone. This relatively thin layer of the fossa makes up the roof of each orbit. Finally, on both sides of the posterior portion of the anterior cranial fossa, there is an optic canal, which is a passageway for the ophthalmic arteries and optic nerves to travel to the orbit.

The floor of the anterior cranial fossa can give rise to skull base meningiomas, which may involve the optic canal and impinge upon the optic nerve producing visual loss. In addition, skull base fractures may involve the anterior cranial fossa. Major areas of vulnerability include the cribriform plate and the roof of the orbit. If the roof of the orbit is fractured, known as a superior blow-out fracture or blow-in fracture, intraorbital contents may protrude into the anterior cranial fossa.

Further Reading

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Anterior Crocodile Shagreen

► Mosaic Degeneration (Anterior Crocodile Shagreen)

Anterior Embryotoxon

► Corneal Arcus

Anterior Eye Segment Surgery

► Anterior Segment Surgery

Anterior Inferior Cerebellar Artery

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Synonyms

AICA

Definition

The anterior inferior cerebellar artery (AICA) is a branch of the basilar artery. AICA travels across the pons to the cerebellopontine angle, where it lies adjacent to cranial nerves VII and VIII, proceeds to the internal auditory meatus, and travels along the surface of the cerebellum. It supplies the anterolateral cerebellum, parts of the pons, and the labyrinth in the inner ear. AICA sometimes has connections with the posterior inferior cerebellar artery (PICA) as well as the superior cerebellar artery (SCA). AICA can be divided into three segments: the premeatal segment, meatal segment, and postmeatal segment. The premeatal segment extends from the origin of the vessel to cranial nerves VII and VIII, the meatal segment is the part proceeding to the internal auditory canal, and the post meatal segment travels along the cerebellum. The AICA has several branches that supply different sections of the brain. The internal auditory artery (labyrinthine artery) travels with cranial nerves VII and VIII to the internal auditory meatus and is the sole blood supply to the labyrinth. In 50% of people, the labyrinthine artery arises from the AICA, but it may arise from the basilar artery as well. The subarcuate artery supplies the bone in the semicircular canals. There are also cerebellar cortical branches that supply the anterolateral cerebellum, as well as perforating branches that supply the brainstem.

Ischemia in the distribution of the AICA may cause vertigo, vomiting, hearing loss, facial palsy, and ipsilateral limb ataxia. For ophthalmology, these signs and symptoms may be associated with problems with gaze-holding and pursuit or vestibular nystagmus. The ocular motor signs may be due to involvement of the labyrinth, vestibular nuclei, or cerebellar flocculus.

Cross-References

► Nystagmus

References

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Anterior Lamellar Keratoplasty (ALK)

► Lamellar Keratoplasty

Anterior Lamellar Keratoplasty, Laser Assisted

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Synonyms

Femtosecond laser-assisted lamellar keratoplasty

Definition

Keratoplasty by programming the femtosecond laser to create bladeless, precise anterior lamellar interface, and peripheral trephination cuts with certain depths and diameters. The applanation lens which is used for LASIK flaps is also used in the laser-assisted anterior lamellar keratoplasty. Laser-assisted lamellar keratoplasty is used in eyes with pathology limited to the anterior layers such as keratoconus, corneal problems after laser in situ keratomileusis (ectasia), and corneal stromal opacities.

Epidemiology

Femtosecond laser-assisted anterior lamellar keratoplasty has already been performed in humans with good visual outcomes and is becoming an interesting and accurate alternative to non-laser keratoplasty.

History

In 2008, Yoo et al. described the use of a femtosecond laser in lamellar keratoplasty for anterior corneal pathology. Due to the fact that the femtosecond technology is becoming more and more common in several corneal procedures, this method is gaining significant weight because of its efficacy, safety, and accuracy.

Clinical Features

The femtosecond laser is a 1053 nm wavelength laser that generates pulses in the femtosecond range. This results in minimal surrounding tissue damage during the process called photodisruption. The laser vaporizes small amounts of the tissue, and a plasma and shock wave formation is followed by the release of gas and bubble formation in the corneal stroma. A dissection plane is created after many pulses have been applied in the same area within the corneal stroma.

Tests

Thorough examination of the anterior segment with the slit lamp and corneal topography, pachymetry, and measurement of uncorrected and best spectacle-corrected visual acuity are mandatory to maintain the best possible postoperative results. See also entries "► Anterior Lamellar Keratoplasty (ALK)," "► PRK," "► Laser Speckle," and "► Wavefront-Guided LASIK."

Differential Diagnosis

Other types of keratoplasty performed by femtosecond lasers:

- Femtosecond laser-assisted posterior lamellar keratoplasty
- Femtosecond laser-assisted penetrating keratoplasty

Etiology

See "History" section above.

Treatment

Primarily the femtosecond laser cut is created on both donor and recipient corneas. The donor lamellar cut has a diameter and thickness which are determined by the corneal opacity which has to be removed. After using topical anesthesia, a suction ring is positioned at the sclerolimbal margin to stabilize the eye. The trephination cut is performed by programming a circular pattern of laser sports which move in a defined direction, with starting points in the lamellar interface and ending points. Energy settings for the lamellar interface and trephination cuts are similar to those used in standard LASIK. The host corneal button is then removed and replaced with the donor lamellar button on the recipient residual corneal stromal bed. Finally, a bandage contact lens is fitted on the cornea, and the patient is placed on antibiotic and steroid eye drops.

Cross-References

- ▶ Femtosecond Laser
- ▶ Free Caps, LASIK Complication
- ▶ Nd:YAG Laser

Further Reading

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Soong et al (2008) Femtosecond laser-assisted lamellar keratoplasty. Arq Bras Oftalmol 71(4):601–606

Yoo et al (2008) Femtosecond laser-assisted sutureless anterior lamellar keratoplasty. Ophthalmology 115:1303–1307

Anterior Limiting Membrane Dystrophy, Type I (ALMD I)

▶ Reis-Bücklers Dystrophy

Anterior Limiting Membrane Dystrophy, Type II

▶ Thiel-Behnke Dystrophy

Anterior Megalophtalmos

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Synonyms

X-linked megalocornea

Definition

A congenital condition presenting with large corneal diameter (>13 mm) and a very deep anterior chamber (>4 mm), first described by Kayser (1914).

Etiology

An underlying genetic defect has been localized on the long arm of the X chromosome in a single family (Chen et al. 1989). Most likely, persistence of the early embryonic relationship between the diameter of the anterior opening of the eye cup and the equatorial diameter leads to a large cornea and deep anterior chamber (Mann 1957). The hypothesis that an increased intraocular pressure

is the principal cause was abandoned because characteristic bridges of iris tissue found in patients with anterior megalophthalmos were also found in a large portion of normal eyes.

Clinical Presentation

A large corneal diameter (13–14.5 mm, symmetrical in both eyes), a deep anterior chamber (4–6 mm), and an iris hypoplasia with transillumination defects are characteristic for eyes with anterior megalophthalmos (Meire 1994). In the majority of cases, visual acuity is not significantly affected but could be reduced by the development of cataract and central corneal mosaic dystrophy. The refraction is mostly emmetropic. Astigmatism can be present but is not obligate. Characteristically, the patients develop an arcus lipoides during their third decade of life. Gonioscopy reveals a wide angle and a heavily pigmented trabecular meshwork, often with bridges of iris tissue. Other clinical features developing later are pigment dispersion and dislocation of the crystalline lens. Axial length is increased in most eyes, mainly due to an enlargement of the anterior segment.

Diagnostics (Lab Diagnostics)

An underlying genetic defect has been localized on the long arm of the X chromosome. In families with X-linked megalocornea, DNA analysis can help to detect female carriers. DNA analysis may also help to resolve the question of whether or not a male with large corneal diameters in a family with proven X-linked megalocornea is affected.

Differential Diagnosis

Anterior megalophthalmos needs to be discriminated from other conditions with large corneal diameters and high anterior chamber depths such as simple megalocornea or megalophthalmos. Megalophthalmic eyes typically show an excessive myopia due to a high vitreous length. In infants, it is extremely important to rule out a buphthalmus due to congenital glaucoma.

Prophylaxis

There is no prophylaxis of the condition itself. However, patients should be monitored closely to prevent complications of the condition such as glaucoma, cataract, and lens subluxation.

Therapy

There is no therapy of the condition itself. However, patients should be monitored closely to prevent complications of the condition such as glaucoma, cataract, and lens subluxation.

Prognosis

The prognosis is good. Cataract, glaucoma, and in some cases the mosaic dystrophy might affect visual acuity.

Epidemiology

Anterior megalophthalmos is a rare condition with less than 100 cases reported so far. However, the real prevalence might be higher.

Cross-References

▶ Megalocornea
▶ Microphthalmos

References

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Anterior Megalophthalmus

► Keratoglobus Basic Science

Anterior Optic Capture

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Synonyms

ACCC–OC; Anterior CCC optic capture

Definition

The optic capture describes a capsular fixation technique performed in pediatric cataract surgery and placed in intraocular lens (IOL) complication and management. Especially the anterior optic capture is performed while a dislocated IOL sits preoperatively behind the capsule in the anterior vitreous.

Indication

The indication for an optic capture is given in pediatric patients to reduce posterior capsular opacification and rotationally stable of the IOL. Another indication is given in subluxed intraocular lenses to reposition. The position of the intraocular lens preoperatively affects the decision to proceed with anterior or posterior optic capture.

Contraindication

In the absence of a good anterior capsule shelf and no major zonular defects, a capsular fixation technique is not feasible.

Techniques and Principles

The optic sits anterior to the capsulorhexis and the haptics behind the capsule. Inversely the haptics lie in the ciliary sulcus, and the optic is posterior to the capsular remnant. The position of the intraocular lens preoperatively affects the decision to proceed with anterior or posterior optic capture.

In case a subluxed IOL must be secured by microgaspers in one hand, the IOL may further dislocate onto the posterior pole. In the mean time, an anterior chamber maintainer should be placed in a corneal incision to maintain the intraocular pressure.

Outcome

The success depends on the specific indication and location of a subluxed lens.

Complications

In case of a subluxed IOL, there is a risk of IOL's dislocation onto the posterior pole necessitating of a retinal surgeon. An elective optic capture in pediatric eyes includes the general risks of cataract surgery.

History

Reference is made to the respective techniques.

Clinical Features

Depending on the method, different instruments are needed. In the following, the vitrector, the cystotome, the capsulorhexis forceps, the aspiration handpiece, and the Fugo plasma blade tip are to be mentioned.

For details, it is referred to especially written articles.

Cross-References

► Anterior Capsulorhexis
► Cataract Surgery

► Continuous Curvilinear Capsulorhexis (CCC)
► Intraocular Lens
► Secondary Cataract

References

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Anterior Orbitotomy

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Definition

A surgical procedure to access a specific area of the anterior orbit, generally considered to be within the anterior two-thirds of the orbit.

Purpose

To provide the most direct route either transcutaneously or transconjunctivally to the anterior orbit, keeping in mind normal anatomical structures (blood vessels, nerves, muscles, etc.) that may be nearby (Levine 2003; Nerad 2001).

Principle

To safely access the anterior orbit.

Indications

To access an area of the orbit for biopsy of a lesion, removal of a lesion, removal of a foreign body, fat or bony orbital decompression (Levine 2003; Nerad 2001).

Contraindication

Area necessary to access is not in the anterior orbit. Any medical contraindication to surgery.

Classification

Orbital surgery/Orbitotomy

Advantages/Disadvantages

Safe approach to anterior lesions/requires surgical intervention.

Cross-References

► Graves Ophthalmopathy
► Orbital Pain

References

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Nerad JA (ed) (2001) Oculoplastic surgery. The requisites in ophthalmology. Mosby, St. Louis, pp 387–418

Anterior Radial Keratotomy

► Radial Keratotomy

Anterior Segment

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Definition

The anterior segment of the eyeball comprises the cornea, iris, ciliary body, and lens.

Cross-References

▶ Anterior Segment Partial Coherence Interferometry

Anterior Segment Dysgenesis

▶ Microphthalmos (Microphthalmia), Anterior

Anterior Segment Optical Biometry

▶ Anterior Segment Partial Coherence Interferometry

Anterior Segment Optical Coherence Tomography

▶ Computerized Corneal Topography

Anterior Segment Partial Coherence Interferometry

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Synonyms

Anterior segment optical biometry

Definition

Anterior segment partial coherence interferometry is an optical biometry of intraocular distances in the eye from the cornea to the back of the lens.

Purpose

Anterior segment partial coherence interferometry allows precise measurement of central corneal thickness, anterior chamber depth, and lens thickness.

Principle

In dual-beam partial coherence interferometry, a Michelson interferometer splits an infrared light beam of high spatial coherence but very short coherence length into two parts, forming a coaxial dual beam. This dual light beam, containing two beam components with a mutual time delay of twice the interferometer arm length difference introduced by the interferometer, illuminates the eye. Both components are reflected at several intraocular interfaces that separate media of different refractive indices. If the delay of these two light beam components produced by the interferometer equals an intraocular distance within the coherence length of the light source, an interference signal (called partial coherence interferometry signal) is detected, similar to that of ultrasound A-scan.

Indication

Optical biometry of the anterior segment of the eye prior to cataract or refractive surgery.

Contraindication

Patients with dense cataracts or patients unable to cooperate or fixate during the measurement process.

Advantage/Disadvantage

Anterior segment partial coherence interferometry is a precise and reliable method for biometry of the anterior segment of the eye. In contrast to ultrasound contact biometry, the measurement is

independent of the examiner's ability to locate the correct position of the eye during measurement. In contrast to ultrasonic biometry, noncontact anterior segment partial coherence interferometry reduces the risk of injuring the cornea during measurement. However, in contrast to ultrasound biometry, lens thickness cannot be assessed in patients with dense cataracts or opaque media.

Cross-References

- ▶ Anterior Segment
- ▶ Optical Biometry
- ▶ Partial Coherence Interferometry

Further Reading

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Anterior Segment Surgery

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Synonyms

Anterior eye segment surgery

Definition

Summary of all recent events in anterior eye segment surgery. These surgical interventions include the area of lens, corneal, refractive, glaucoma, and squint surgery.

Epidemiology

Anterior segment surgery is still a growing and innovating range in ophthalmological treatment. Especially by the cataract surgery and an increasing number of refractive operative treatment, procedures of the anterior eye segment form the main part.

History

Reference is made to the respective article section.

Clinical Features

Reference is made to the respective article section.

Tests

Preoperative tests should include in addition to the efficient patient's anamnesis (drugs, past eye interventions, general diseases, familiar eye diseases) the systematic examination of anterior segment and fundus (dilated pupil) in both eyes to preclude several exclusion criteria.

The special diagnostics and including and excluding criteria depend on the type of surgery.

Differential Diagnosis

See "Treatment" section bottom.

Etiology

See "History" section above.

Treatment

The majority of anterior segment surgery is made in cataract and corneal surgery.

These days, cataract surgery technique includes phacoemulsification, ECCE, and ICCE with implantation of artificial lenses.

Corneal surgery comprehends refractive surgery and cornea transplantation. Specifically, these are mainly laser surgical procedures, phacic intraocular lenses, refractive lens exchange, UV-cross-linking, astigmatic keratotomy, and limbal relaxating incision. In the field of cornea transplantation today, there are opportunities to transplant perforating or laminating.

Cross-References

- ▶ Cataract Surgery
- ▶ Cornea Plana
- ▶ Corneal Topography
- ▶ Infantile Glaucoma
- ▶ Laser Speckle
- ▶ Refractive Surgery

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Anterior Vitrectomy

- ▶ Vitrectomy

Anterior Vitreous Detachment, Contusion Injury Causing

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Synonyms

Vitreous base avulsion, "bucket-handle sign"; Vitreous base detachment

Definition

Contusive ocular injury may avulse the vitreous base from its firm adhesion spanning the ora serrata. In fact, vitreous base avulsion is considered pathognomonic for ocular contusion injury.

Etiology

Contusive ocular injury may damage posterior segment structures by several mechanisms. The severity varies from self-limited commotio retinae to vision-threatening retinal detachment. The vitreoretinal interface plays a key role in the pathophysiology of most retinal injuries. Retinal detachment is often the final common pathway for traumatic disruption of the pars plana, vitreous base, or retina.

The vitreous most tightly adheres to the retina at the vitreous base, a band of condensed vitreous that spans the ora serrata 360°. The vitreous base extends approximately 2 mm anterior to the ora serrata and 2–4 mm posteriorly. This tight interface plays a major role in the

pathophysiology of traumatic retinal breaks and detachments.

Blunt trauma rapidly compresses the eye along its anteroposterior axis and expands it in the equatorial plane, resulting in severe traction on the vitreous base that may detach it. Although the vitreous base can be avulsed from the underlying retina and nonpigmented epithelium of the pars plana without tearing either one, usually one or both are also torn in the process.

Vitreous base avulsion has also been reported spontaneously in young patients with inferotemporal retinal dialysis, in a patient with neurofibromatosis, and as a presenting sign of child abuse.

Clinical Presentation

Contusive trauma stresses the vitreoretinal interface and vitreous base, increasing the risk of vitreoretinal interface separation. The trauma associated with vitreous base avulsion is often presumed severe considering the vitreoretinal adhesions are often strongest at the vitreous base. Consequently, avulsion without concomitant pars plana tears, retinal dialyses, or retinal tears is uncommon. Dialyses are usually located at the posterior border of the vitreous base but can also occur at the anterior border and usually occur due to blunt ocular trauma. Vitreous base avulsion is also commonly associated with iris trauma or hyphema.

Patients with an isolated vitreous base avulsion following blunt trauma may present with blurred vision and/or a "stringy" floater in the eye. In many cases it may be asymptomatic.

A special consideration should be given to trauma in young eyes. Although young patients have a higher incidence of eye injury than other age groups, only in rare instances does the retina detach immediately following blunt trauma because young vitreous has not yet undergone syneresis or liquefaction. The vitreous, therefore, provides an internal tamponade for the retinal tears or dialyses. With time, however, the vitreous may liquefy over a tear, allowing fluid to pass through the break to detach the retina. The clinical presentation of the retinal detachment is thus usually delayed, with only 12% of detachments identified immediately, 30% identified within 1 month, 50% identified within 8 months, and 80% identified within 24 months.

Diagnosis

Vitreous base avulsions appear as a stripe of translucent vitreous overlying the peripheral retina or ora serrata, creating a "bucket-handle" appearance. The presence of this finding should warrant a careful examination of the pars plana, ora serrata, and retinal periphery when the eye becomes stable enough for scleral depression.

In the acute setting, examination may be limited by the severity of injury, patient discomfort, and clarity of ocular media. Determination of pupillary light reaction and evaluation for a relative afferent pupillary defect should be performed in all cases. During the posttraumatic period, every patient should receive a complete ocular examination.

Differential Diagnosis

NA

Prophylaxis

Limited to wearing ocular protection (e.g., during sports activities)

Therapy

This condition may be asymptomatic and requires no treatment or surgical intervention if found in isolation. Close follow-up is recommended until

the ora serrata and pars plana area can be adequately visualized to rule out retinal dialysis or tears of the pars plana.

Prognosis

When isolated, vitreous base avulsion usually has no serious ocular consequences. However, prognosis varies in the presence of associated ocular pathology such as retinal tears, retinal dialysis, iris trauma, or hyphema, respectively.

Epidemiology

Much of the reported epidemiologic information regarding contusive posterior segment injury focuses on traumatic retinal detachment, a final common pathway for most posterior segment injuries. Traumatic retinal detachments account for between 10% and 19% of all aphakic retinal detachments. Trauma contributes to the peak incidence in younger years (20–29 years of age). Eighty percent of traumatic detachments occur prior to the age of 40. Men outnumber women in traumatic detachment (78% vs. 22%).

Vitreous base avulsion has been reported in 25.9% of patients with traumatic retinal detachment. Vitreous base avulsions have been reported to occur in roughly half of patients with retinal detachments secondary to squash ball injuries.

Cross-References

► Blunt Trauma
► Vitreous Base Detachment

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Anti-angiogenesis

► Antivascular Endothelial Growth Factor

Antibiotics for Eye Infections

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Definition

Substance or compound produced by a microorganism that kills other microorganisms or inhibits their growth.

Indication

Prophylaxis or therapy of infections of the eye and orbit caused by bacteria, fungi, or protozoans.

Contraindication

Allergy or intolerance to antibiotics.

Use and Dosage

Antibiotics differ in pharmacokinetic and pharmacodynamic and may either be applied as topical (eyedrops), oral, intravenous, or intracameral or intravitreal injection.

Adverse Reactions

Depending on the antibiotics used and the microbial organisms targeted.

Interactions

Depending on the antibiotics used.

Cross-References

- ▶ Cefuroxime
- ▶ Intracameral Antibiotics
- ▶ Keratitis

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Anticoagulant Medication

- ▶ Anticoagulants, Ophthalmological Treatment

Anticoagulants, Ophthalmological Treatment

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Synonyms

Anticoagulant medication; Decoagulants

Definition

Anticoagulants (Greek: anti, against; Latin: coagulation, agglomerate) are drugs used to arrest the blood coagulation. Based on the mechanism of action, we distinguish direct and indirect anticoagulants.

Medicinal products, for example, include heparin and derivative substances, coumadins (antidot, vitamin K), prostaglandin synthesis inhibitors, fibrinolytics, and tissue plasminogen activators.

Indication

A prophylactic indication is given, for example, in preventing thromboses or pulmonary embolism. A therapeutic indication is given in atrial fibrillation or atrial flutter, thromboses, or postoperative protection (heart valve replacement). Some chemical compounds are used in medical equipment.

Especially in ophthalmological treatment, anticoagulants are cardinally used in the treatment and prophylaxis of retinal artery or vein occlusion syndromes, chemical alkali burn, infective corneal ulcer, and keratitis filiformis.

Further anticoagulant ointment (containing heparin) is, for example, applied to bruising and swelling in the area of the eye. A systemic and intraocular injected use of heparin was also described in case of intraocular fibrine.

Contraindication

Contraindications vary between the different preparations of anticoagulant drugs, which generally include bleeding (especially intracranial), fresh wounds and incisions, gastrointestinal ulcer, arterial hypertension, chronic alcoholism, hemophilia, pregnancy, and severe liver and kidney diseases.

Use and Dosage

Because of the diversity of preparations of topical and systemic application in anticoagulation therapy, reference is made at this point to specific textbooks of pharmacology.

In case of sytemical appliance, it should be attended to internal medicine cooperation.

Adverse Reactions

An overdose may cause the risk of bleeding (internal organs, brain). Especially on the eye bleeding of vitreous body and hyposphagma have to be mentioned.

The effect of anticoagulants is persists about several days and should be remembered in case of surgeries (especially elective interventional treatment).

Interactions

A coadministration of salicylic acid and coumarins should be avoided. An increased effect of oral anticoagulants is seen in combination with medications that affect liver enzymes (inhibition or induction).

Interactions were also described in combination with intravenous cephalosporins and oral sulfonylureas.

In addition to that, vitamin K-rich foods should be eaten only in small quantities to prevent a reduction of the effect.

Cross-References

- ▶ Central Retinal Artery Occlusion, Ocular Ischemic Syndrome
- ▶ Central Retinal Vein, Occlusion of
- ▶ Hyposphagma
- ▶ Neovascular Glaucoma in Ocular Ischemia, Others
- ▶ Vitreous Humor

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Anti-neovascular

- ▶ Antivascular Endothelial Growth Factor

Antioxidants

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Definition

Antioxidants are protective factors against age-related macular degeneration (AMD). They may include zinc, beta-carotene, vitamin C and E, lutein/zeaxanthin, omega 3 fatty acid, and eicosapentaenoic/docosahexaenoic acid.

Indication

According to The Age-Related Eye Disease Study (AREDS) that was sponsored by the US National Eye Institute taking high levels of antioxidants and zinc can reduce the risk of developing advanced age-related macular degeneration (AMD) by about 25%. Additional research suggests that carotenoids and antioxidant vitamins may help to retard some of the destructive processes in the retina and the retinal pigment epithelium that lead to age-related degeneration of the macula. From these findings, it is recommended that antioxidants are indicated in people who are at high risk for developing advanced AMD.

Contraindication

Allergy to any of the substances.

Use and Dosage

The specific daily amounts of antioxidants and zinc used by the study researchers were vitamin C 500 milligrams (mg); vitamin E 400 International Units (IU); 15 milligrams of beta-carotene (often labeled as equivalent to 25,000 International Units of vitamin A); zinc as zinc oxide 80 mg; and 2 mg of copper as cupric oxide. The reason copper was added to the AREDS formulations containing zinc was to prevent copper deficiency anemia, a condition associated with high levels of zinc intake. There are a number of commercial formulas and patients are advised to follow the manufacture recommended manufacturer instructions.

Adverse Reaction

Beta-carotene may slightly increase the risk of cancer in patients that are heavy smokers as seen in studies by National Cancer Institute. AREDS2 showed it is possible to replace beta-carotene from the original AREDS formulation with lutein/zeaxanthin; it may decrease the risk of lung cancer in smokers. Vitamin E in excess of 400 IU is no longer protective and may exacerbate prostate cancer.

Interaction

Antioxidants interact with radiotherapy and certain forms of chemotherapy. It is recommended to have a four half-life separation used concurrently.

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Antivascular Endothelial Growth Factor

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Synonyms

Aflibercept; Anti-angiogenesis; Anti-neovascular; Aptamer; Bevacizumab; Monoclonal antibody; Pegaptanib; Ranibizumab; VEGF Trap-eye

Definition

History

In 1948, Isaac Michaelson posited that a diffusible, hypoxia-induced "factor X" was released by nonperfused retina and caused angiogenesis. Judah Folkman later studied tumor vasculature and hypothesized that tumors secrete a diffusible, angiogenic growth factor which he termed "tumor angiogenesis factor (TAF)." He also suspected TAF was important in ocular neovascularization and theorized that angiogenesis inhibitors could be used to treat cancer and other angiogenesis-dependent diseases. In the 1980s, two groups separately described what we now know as vascular endothelial growth factor (VEGF). Dvorak and Senger described an inducer of vascular leakage and vascular permeability factor (VPF), and Napoleone Ferrara identified angiogenic VEGF. It was not until 1993, however, that Ferrara created an antibody against VEGF and proved it reduced

angiogenesis and decreased experimental tumor growth (Das and Friberg 2011). Since then, the advent of anti-VEGF therapy has greatly expanded the armamentarium for treating many cancers and vascular-mediated diseases of the eye.

VEGF, among other factors, is a key component in ocular angiogenesis, microvascular permeability, and endothelial cell survival. It is a family of isoforms that includes VEGF-A, VEGF-B, VEGF-C, VEGF-D, VEGF-E, platelet-derived growth factor (PDGF), and placental growth factor (PlGF). Alternative splicing of the human VEGF-A gene yields six principal isoforms, one of which is $VEGF_{165}$ (Nguyen et al. 2010). $VEGF_{165}$ is the most potent and prevalent among the major forms expressed during pathologic neovascularization (Das and Friberg 2011).

A variety of pathologic ocular conditions result in vision loss due to abnormal blood vessel growth. Several strategies to inhibit the action of VEGF have been explored, originating mainly in the oncology field. In ocular neovascularization, neutralizing anti-VEGF antibodies, like ranibizumab and bevacizumab, and soluble fusion proteins, like aflibercept, are the most popular treatment options. Other agents investigated include tyrosine kinase inhibitors (pazopanib, vatalanib), inhibitors of protein kinases (ruboxistaurin, sirolimus), small interfering RNA (siRNA) molecules (bevasiranib, PF-04523655) (Das and Friberg 2011), and a novel agent, squalamine, that uses the modulatory protein calmodulin to inhibit VEGF, PDGF, and bFGF.

Anti-VEGF Therapies

In 2003, clinical trials involving a humanized form of an anti-VEGF monoclonal antibody, bevacizumab (Avastin, Genentech), showed extended median survival time for patients with colorectal cancer. The FDA approved bevacizumab in 2004 for the treatment of metastatic colorectal cancer. It was soon realized that anti-VEGF therapy could also be used to target ocular angiogenesis (Das and Friberg 2011).

The initial studies with anti-VEGF therapy in the eye were directed toward the presence of choroidal neovascularization (CNV) in age-related macular degeneration (AMD). It has been shown that CNV removed with surgery is strongly reactive with anti-VEGF antibody and pharmacologic inhibition decreases experimental laser-induced CNV in animal studies (Das and Friberg 2011). Ocular VEGF levels have also shown to be elevated in other diseases of ocular neovascularization, including retinal vein occlusion, diabetic retinopathy, diabetic macular edema, neovascular glaucoma, rubeosis, and retinopathy of prematurity. Furthermore, studies have shown a correlation between intraocular VEGF levels and activity of neovascularization in diseases like proliferative diabetic retinopathy and central retinal vein occlusion (Nguyen et al. 2010).

Since then, multiple trials have investigated the safety and efficacy of various anti-VEGF therapies in ocular diseases. The original ocular anti-VEGF therapy, pegaptanib (Macugen, Eyetech), binds only the 165 kD form of VEGF, while the well-known monoclonal antibodies, ranibizumab (Lucentis, Genentech) and bevacizumab (Avastin, Genentech), bind all biologically active forms of VEGF-A. Aflibercept (Eylea, Regeneron) is a newer recombinant fusion protein with high affinity for VEGF-A, as well as VEGF-B, VEGF-C, VEGF-D, and PDGF.

Approved in 2004, pegaptanib (Macugen, Eyetech) was the first FDA-approved therapy targeting VEGF in patients with neovascular AMD. Pegaptanib is a PEGylated oligonucleotide RNA aptamer with a high binding specificity for only the $VEGF_{165}$ isoform. Compared to antibodies, aptamers are chemically synthesized nucleic acid or peptide oligomers that bind a specific target molecule, acting like a "chemical antibody," and are capable of greater specificity and affinity than antibodies. The VEGF Inhibition Study in Ocular Neovascularization (VISION) trial demonstrated that, after 2 years, those receiving intravitreal pegaptanib for CNV due to age-related macular degeneration (AMD) every 6 weeks were half as likely to lose greater than 15 ETDRS letters than those who stopped (Nguyen et al. 2010). At 2 years, 10% of treated patients gained at least three lines of vision. The

clinical trial results were promising; however, efficacy in the clinic was not dramatic or durable (Das and Friberg 2011).

Ranibizumab (Lucentis, Genentech) was the first monoclonal antibody tested in the treatment of neovascular AMD. Also known as immunoglobulins, antibodies are proteins used to help identify and neutralize objects foreign to the body's immune system. The region of the antibody responsible for binding antigens on that foreign object is the Fab (Fragment, antigen-binding) region. The base of the protein, the Fc (Fragment, crystallizable), is involved in modulating immune cell activity and ensures the appropriate response to the specific antigen. Ranibizumab is a recombinant humanized monoclonal antibody that is a Fab fragment, a refinement of the full-length monoclonal antibody bevacizumab. It differs from pegaptanib in that it binds all active forms of VEGF-A. Specifically developed for intraocular use, it binds VEGF-A with greater affinity than bevacizumab. Also, the absence of the Fc portion when compared to bevacizumab eliminates the possibility of complement-mediated or cell-dependent cytotoxicity and decreases the half-life to minimize extended systemic exposure. Ranibizumab was approved by the FDA in 2006. Compared to the previous treatments of conventional laser, photodynamic therapy (PDT), and pegaptanib, it was the first treatment for neovascular age-related macular degeneration that demonstrated overall improvement in visual acuity instead of decreased visual loss.

Bevacizumab (Avastin, Genentech) is another humanized monoclonal antibody directed against VEGF-A. It was initially approved for intravenous use in the treatment of metastatic colon cancer but has since been used off-label for many ocular diseases and has shown good tolerability and improved visual acuity. It is a full-length humanized monoclonal antibody that binds and, similar to ranibizumab, inhibits all biologically active forms of VEGF-A. There was early interest in using bevacizumab in the treatment of neovascular AMD, but animal studies conducted by Genentech comparing a full-length antibody similar to bevacizumab indicated that the radiolabeled full-length antibody did not cross the ILM, whereas the Fab fragment could diffuse through the RPE. However, in 2005, the SANA trial reported improved vision and a reduction in central macular thickness with intravenous bevacizumab in nine patients with neovascular AMD (Moshfeghi et al. 2006). Systemic side effects, including hypertension and thrombosis, however, limit its use systemically, especially in the older population. Soon thereafter, intravitreal administration of bevacizumab proved to be efficacious with fewer systemic side effects (Das and Friberg 2011).

Aflibercept (Eylea, Regeneron) is a newer anti-VEGF therapy first approved by the FDA in 2011 for the treatment of neovascular AMD. It is a 110-kDa soluble recombinant fusion protein that consists of an IgG fragment with copies of extracellular VEGFR domains from VEGFR-1 and VEGFR-2. It has a high affinity for all VEGF-A isoforms in addition to VEGF-B, VEGF-C, VEGF-D, and PDGF and binds VEGF more tightly than the native receptor or monoclonal antibodies.

Indication

The pathogenesis of many retinal disorders is based on neovascularization and increased vascular permeability. AMD was the original target and most studied for use of anti-VEGF therapy. Choroidal neovascularization (CNV) is the hallmark of neovascular AMD and responsible for 90% of cases of severe vision loss due to AMD (Ventrice et al. 2013).

The safety and efficacy of anti-VEGF agents, specifically ranibizumab, has been extensively investigated in clinical trials for neovascular AMD and more recently in trials for diabetic macular edema and retinal vein occlusion. The pivotal studies using ranibizumab in AMD were the MARINA and ANCHOR trials.

The Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular Age-Related Macular Degeneration (MARINA) trial was a 2-year, prospective, randomized, double-masked,

sham-controlled trial to investigate the safety and efficacy of ranibizumab in the treatment of patients with minimally classic or occult neovascular AMD. Patients were treated monthly with 0.5 mg ranibizumab, 0.3 mg ranibizumab, or a sham injection. At the end of 1 year, 95% of patients receiving ranibizumab injections lost fewer than 15 letters compared to 62% of patients receiving sham injections. Similarly, visual acuity improved by 15 or more letters in 24.8% of the 0.3 mg group and 33.8% of the 0.5 mg group compared to 5% of the sham-injection group. This benefit in visual acuity was maintained at 24 months.

The anti-VEGF antibody for the treatment of predominantly classic choroidal neovascularization in age-related macular degeneration (ANCHOR) study showed similar results for patients with predominantly classic CNV. It compared monthly 0.3 mg or 0.5 mg ranibizumab to photodynamic therapy (PDT was administered every 3 months as needed). In the ranibizumab-treated groups, 35–40% of patients gained three or more lines of vision compared to 5.6% of the verteporfin group, and visual acuity improved from baseline by 8.5–11.3 letters compared to a decline of 9.5 letters in the PDT group.

Similarly, early intraocular use of bevacizumab showed improvement in vision and decrease in mean central retinal thickness. However, due to its off-label use, many of the initial studies and data gathered were for ranibizumab only. The two were studied head-to-head for the first time in the Comparison of Age-Related Macular Degeneration Treatment Trials (CATT). These studies evaluated the effect of 0.5 mg ranibizumab compared to 1.25 mg bevacizumab when administered monthly or as needed. At 1 year, the mean gain in visual acuity was similar for both drugs (8.5 in the monthly ranibizumab-treated group and 8 letters in the monthly bevacizumab-treated group), and the mean gain was greater for monthly compared to as needed treatment (6.8 and 5.9 in the ranibizumab and bevacizumab groups, respectively). These results were statistically significant.

The initial trials using aflibercept, Intravitreal Aflibercept (VEGF Trap-Eye) in Wet Age-Related Macular Degeneration (VIEW), studied monthly versus every 2-month dosing (following three monthly injections in a loading phase) of intravitreal aflibercept compared to monthly ranibizumab. All aflibercept treatment groups (0.5 mg monthly, 2 mg monthly, 2 mg every 2 months after three initial monthly doses) proved noninferior and clinically equivalent to monthly ranibizumab injections for the primary endpoint, proportion of patients maintaining vision at week 52 (95.1–96.3% among all aflibercept treatment groups compared to 94.4% for the ranibizumab treatment group). Treatment with aflibercept also resulted in a similar improvement in anatomic measures. Ocular and systemic adverse events were similar across all groups (Das and Friberg 2011).

VEGF inhibitors are currently the gold standard for treatment of neovascular AMD. With more use and research in other diseases, it has also become more prevalent in the treatment of diabetic macular edema, proliferative diabetic retinopathy, retinal vein occlusion, non-AMD choroidal neovascularization (idiopathic, inflammatory, myopic, angioid streaks), retinopathy of prematurity, and neovascular glaucoma, among others.

Specifically, ranibizumab is currently FDA-approved for the treatment of patients with neovascular AMD, macular edema following retinal vein occlusion, and diabetic macular edema. Aflibercept is also approved for the same indications. Bevacizumab is still used off-label by many for a variety of ocular diseases with pathologic neovascularization.

In exudative macular diseases, visual gain and stability is expected instead of slowing of vision loss. While monotherapy with anti-VEGF agents is currently the gold standard in many of these diseases, researchers believe there is room for improvement, and investigative approaches look to increase the durability of treatments (decreasing the number of injections), increase efficacy, and minimize scarring. Specifically, current trials are investigating the use of Fovista (Ophthotech), an anti-PDGF agent used in combination with anti-VEGF therapy for the treatment of neovascular AMD. Fovista is designed to allow stripping of pericytes from around blood vessels, thereby leaving the underlying endothelial cells

more vulnerable to anti-VEGF action. Early reports are promising.

Upcoming studies will help determine the optimal dosing frequency, follow-up interval, method of administration, and role of concurrent and novel therapies.

Contraindication

Treatment with intravitreal anti-VEGF agents is contraindicated in patients with active ocular or periocular infections and known hypersensitivity to components of the medication or drug formulation.

Caution is recommended when treating pregnant or nursing patients. No studies have been conducted using ranibizumab or other intraocular anti-VEGF agents in pregnancy. Based on the mechanism of action, treatment may pose a risk to embryo-fetal development. It is not known if drug is excreted in human breast milk.

Use and Dosage

Procedure

Currently, all ocular anti-VEGF therapies are administered intravitreally. Preinjection use of topical antibiotics has been theorized to minimize bacterial flora around the surgical entry site and to have a synergistic effect with preinjection povidone-iodine placement, but this has not been clinically proven, and its use has declined in the last several years. In 2013, 78.2% of respondents of the American Society of Retina Specialists (ASRS) Preferences and Trends (PAT) survey reported not using an antibiotic with intravitreal injections.

Adequate topical anesthesia should be used prior to the injection. Options vary from topical proparacaine drops or soaked pledgets, viscous lidocaine or tetracaine jelly, or subconjunctival injection of lidocaine. The site of the injection is then isolated, and the needle, most commonly 30 or 32 gauge, is placed either 3.5 mm (pseudophakic eyes) or 4 mm (phakic eyes) posterior to the limbus. Prior to the injection, topical application of 5% povidone-iodine is strongly recommended. Proper eyelid hygiene with or without a scrub, sterile drape, and/or speculum is also encouraged.

The role of postinjection antibiotics is controversial. Fourth-generation topical fluoroquinolones were frequently used for a few days postinjection until the conjunctival and scleral openings were healed. No study, however, has demonstrated that pre- or postinjection topical antibiotics reduce the risk of endophthalmitis. In addition, recent studies report a significant increase in the resistance of ocular flora and a greater risk of endophthalmitis with use of topical antibiotics (Falavarjani and Nguyen 2013). Without evidence supporting the use of antibiotics, and new concerns over increasing resistance, many physicians have stopped prescribing them regularly (Nguyen et al. 2010).

Dosing

Unlike other systemic medications, the FDA-recommended dose (Table 1) is sufficient to neutralize elevated intraocular VEGF concentrations and is not dependent on the patient's age, gender, or renal function (Nguyen et al. 2010).

The early trials using intravitreal ranibizumab showed a treatment benefit with monthly injections compared to as-needed, or PRN, injections for neovascular AMD. However, the requirement for

Antivascular Endothelial Growth Factor, Table 1 Currently approved intravitreal anti-VEGF medications and dosing

	AMD	RVO	DME
Ranibizumab	0.5 mg monthly	0.5 mg monthly	0.3 mg monthly
Aflibercept	2 mg monthly first 3 injections then every 2 months	2 mg monthly	2 mg monthly first 5 injections then every 2 months

Bevacizumab is used at doses 1.25–2.5 mg (not FDA-approved for ocular use)

long-term monthly injections has proven to be a burden to patients, families, and physicians alike. Alternative dosing strategies have been and are still being investigated to decrease the treatment burden but maximize the benefit to the patient.

The PIER study evaluated 0.3 mg and 0.5 mg ranibizumab monthly for 3 months followed by quarterly dosing for 24 months. At 12 months, the mean change from baseline was a loss of 1.6 letters and 0.2 letters for the ranibizumab-treated arms, respectively. The sham arm lost 16.3 letters, proving that quarterly treatment decreased leakage from CNV but that the effect was not as robust as monthly treatment. The Prospective OCT Imaging of Patients with Neovascular ARMD Treated with Intraocular Lucentis (PrONTO) study looked at three monthly injections of 0.5 mg ranibizumab as a loading dose followed by PRN treatment based on OCT. At month 24, the mean visual acuity improved by 11.1 letters and improved by 15 letters or more in 43% of patients with an average of 9.9 injections. This study showed that less than monthly treatment can still yield a good visual outcome. Limitations of this study included sample size (40 patients) and the nonrandomized, noncontrolled nature of the study.

The future of anti-VEGF treatment will likely involve an individualized treatment plan for each patient, using OCT to help guide treatment and allowing for fewer injections over time. The popular treat-and-extend regimen used in clinic theoretically decreases the burden to the patient without compromising visual function; however, no large, prospective, multicenter clinical trial comparing the regimens has yet been published.

Adverse Reactions

Since VEGF has emerged as a key target for therapy, use of intravitreal anti-VEGF agents has been widely employed to reduce disease progression and improve visual outcomes. Intravitreal injections, when performed correctly, are generally safe and well tolerated. The complications related to injections have been thoroughly studied in many clinical trials and appear comparable across all treatment groups.

Each injection poses a risk of complication, including infection, inflammation, increased intraocular pressure, vitreous hemorrhage, retinal detachment, and cataract, among others (Ventrice et al. 2013). Nonserious ocular side effects include pain, floaters, chemosis, and subconjunctival hemorrhage. Serious systemic adverse events, including thromboembolic events, have also been reported.

Endophthalmitis is a serious ocular adverse event related to intravitreal injections, reported to occur in 0.019–1.6% in clinical trials, although more recent studies have quoted a lower incidence. In a review by Van der Reis, the incidence of endophthalmitis was below or equal to 0.04 and 0.05 per 100 injections for ranibizumab and bevacizumab, respectively. This included both infectious and noninfectious cases of endophthalmitis (Van der Reis et al. 2011).

The rate of endophthalmitis appears to be the same among different agents, injection settings, and geographic settings. Special attention should be paid to an aseptic preparation and injection procedure, as infection is likely due to contamination of the injection field by aerosolization or droplet spread (Falavarjani and Nguyen 2013). Sterile intraocular inflammation can also be seen after injection and is important to differentiate from infectious endophthalmitis. The time to presentation, presence of pain, and severity of clinical findings may be helpful. However, if endophthalmitis is suspected, intravitreal antibiotics should be administered.

Rhegmatogenous retinal detachment is another adverse event of intraocular injections. It has a low overall incidence rate of 0–0.67% (Falavarjani and Nguyen 2013), with other reviews reporting 0.01 and 0.07 per 100 injections for ranibizumab and bevacizumab, respectively (Van der Reis et al. 2011). It is thought to be due to induction of a posterior vitreous detachment or an incorrect injection technique.

Elevated intraocular pressure (IOP) after intravitreal injection is usually self-limited; however, patients with preexisting glaucoma have higher rates of IOP elevation than those without glaucoma, and there may be persistent elevated IOP over time. Multiple theories have been

proposed for the possible cause of persistent IOP elevation, including a pharmacologic effect of VEGF blockage, inflammation of the trabecular meshwork, impaired outflow due to protein aggregates or silicone debris, and damage to the outflow pathway (Falavarjani and Nguyen 2013). Routine IOP monitoring should be performed in all patients undergoing treatment with anti-VEGF therapy.

Ocular hemorrhage, including subconjunctival hemorrhage, vitreous hemorrhage, and retinal hemorrhage, is another complication of injection. The rates of subconjunctival hemorrhage are higher for those patients taking aspirin, and choroidal hemorrhage and subretinal hemorrhage have also been reported after intravitreal injections. However, given the risk of thromboembolic events, discontinuation of anticoagulants to avoid these adverse events is not recommended (Falavarjani and Nguyen 2013).

Other ocular events are related more to the ocular disease process than the injection itself. For patients with neovascular AMD, RPE tears may occur spontaneously or after therapeutic intervention. The reported incidence after anti-VEGF treatment is 0.06–27%, which may be higher than in the natural course of the disease process. Preexisting RPE detachment is considered a major risk factor, with large PED diameter and vertical height on OCT as predictive indicators. However, a recent study on three major AMD trials showed no statistical significance over 2 years in patients treated with ranibizumab compared to control. In patients who do suffer from an RPE tear, better visual outcomes are observed in those treated with anti-VEGF agents (Falavarjani and Nguyen 2013).

In patients with traction retinal detachment in proliferative diabetic retinopathy, 5.2% of eyes will have progression of the detachment at a mean of 13 days after treatment with intravitreal bevacizumab. There is a similar concern in treating patients with advanced retinopathy of prematurity, and physicians should be ready to operate if progression occurs. Other adverse events reported in patients with diabetes and retinal vein occlusion include decreased retrobulbar flow parameters, retinal arteriolar vasoconstriction, and worsening of macular ischemia.

Rare ocular and systemic side effects have been reported and include anterior ischemic optic neuropathy, retinal vein and artery occlusion, hemorrhagic macular infarction, development or exacerbation of ocular ischemic syndrome, visual hallucination, erectile dysfunction, and acute decrease in kidney function. The causative role of anti-VEGF agents in these cases has yet to be established (Falavarjani and Nguyen 2013).

While treatment is provided locally, systemic adverse events are still a concern. Intravenous administration of bevacizumab has been used widely in treatment protocols for solid cancers. Associated systemic adverse events include thromboembolic events, myocardial infarction, stroke, hypertension, gastrointestinal perforation, and kidney disease. However, the systemic administration of bevacizumab is several hundred-fold greater than the amount administered intravitreally (Moshfeghi et al. 2006).

For intravitreal use, there was a nonsignificant trend in ANCHOR of increased arterial thromboembolic events in the higher 0.5 mg ranibizumab dose study arm. There was also a trend for greater risk of CVA or nonvascular death for higher doses of ranibizumab in the SAILOR study, but this was not statistically significant and patients also had known cardiovascular risk factors (Das and Friberg 2011). Further studies did not demonstrate this increased risk. In CATT, the rates of death and arteriothrombotic events were similar for both bevacizumab and ranibizumab, but the proportion of patients with one or greater serious systemic adverse event was higher in the bevacizumab group. In contrast, IVAN demonstrated both medications to be equivalent in regard to visual improvement, and there was no difference between the drugs with respect to serious adverse events. Because of this trend in data, however, some physicians prefer not to treat patients with recent cerebrovascular accident.

In the review by Van der Reis, systemic adverse events occurred at a rate of 0.05 for bevacizumab and 0.09 for ranibizumab per 100 injections for cardiovascular disease. The incidence rates of CVA and TIA were below or equal to 0.07 per 100 injections. Thromboembolic

events, including nonfatal MI, CVA, and death from a vascular or unknown cause, were 0.07 and 0.18 for bevacizumab and ranibizumab, respectively. Vascular diseases such as deep vein thrombosis, iliac artery aneurysms, and femoral artery thrombosis have also been reported (Van der Reis et al. 2011).

While serious ocular and systemic adverse events do occur, their rates are low. Adverse events may occur due to the procedure itself, the drug, the drug vehicle, or underlying disease mechanism. Safety profiles appear comparable, and the rates of adverse events appear similar with all treatments.

Interactions

Drug interaction studies have not been conducted with intraocular bevacizumab, ranibizumab, and aflibercept.

Cross-References

- ▶ Age-Related Macular Degeneration
- ▶ Central Retinal Vein, Occlusion of
- ▶ Choroidal Neovascularization
- ▶ Diabetic Macular Edema
- ▶ Diabetic Retinopathy, Proliferative
- ▶ Macular Edema
- ▶ Neovascular Glaucoma in Diabetes Mellitus
- ▶ Neovascularization, Retinal
- ▶ Optic Disc in Central Retinal Vein Occlusion
- ▶ Retinal Blood Vessels
- ▶ Retinopathy of Prematurity

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Aphakic Spectacles

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Definition

Eyeglasses prescribed after cataract surgery when no intraocular lens is inserted into the eye. Today, in uneventful cataract surgery, the crystalline lens of the eye is typically replaced by an artificial lens implant. If such a lens cannot be implanted, a thick (plus-powered) convex lens is used to correct strong hyperopia. Such glasses are cumbersome, greatly distort peripheral vision (ring scotoma), and increase lateral magnification which effects a loss of stereo vision in unilateral use.

Cross-References

- ▶ Hyperopia
- ▶ Refractive Errors

Apocrine Cystadenoma

- ▶ Hidrocystoma, Apocrine
- ▶ Sweat Glands of Eyelid, Tumors Arising in

Apocrine or Sweat Glands of the Eyelid

▶ Glands of Krause, Glands of Moll, Glands of Wolfring, Glands of Zeis

Apocrine Retention Cyst

▶ Sweat Glands of Eyelid, Tumors Arising in

Apodized Diffractive Intraocular Lens

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Synonyms

Bifocal intraocular lens; Diffractive intraocular lens; Multifocal intraocular lens

Definition

Intraocular lens using a simultaneous diffractive bifocal optics principle, providing two foci at the same time to enable patients to see clearly in two different distances and apodization to limit peripheral optical phenomena.

Basic Characteristics

Refraction: Diffraction

Light is the visible spectrum of the electromagnetic radiation. Light waves are transverse waves (oscillating perpendicular to direction of propagation) and characterized by wavelength, amplitude, and frequency. Light interacts in several ways with matter. In case of transparent media, light is refracted and reflected. Refraction, however, is a theoretical model and can be explained by Huygens' principle of diffraction. A wavefront is a plane, where a light wave, exposed by the same light source, has the same phase. Huygens' principle states that every point on a wavefront is again the source of another independent wavefront. This way, when a wavefront interacts with an optical surface, a new independent wavefront results. If two or more of such independent wavefronts interact interference appears. The intensity of the resulting wavefront can be increased, decreased, or the wavefront can even be eliminated. Light rays, as used in the theoretical model of light refraction and thus construction schemes of optical system is perpendicular to the tangent of the wavefront. When passing a transparent surface the direction of this perpendicular is changed by diffraction.

Diffractive intraocular lenses use this effect by a defined modification of their surface structure. Usually, circular zones of different thickness are used to enable defined interaction between the incoming and wavefronts by changing the optical path difference. Thus, light propagation in some directions is increased and deleted in others, resulting in two or more foci.

However, about 18% of light is being directed to higher levels of diffraction and thus lost for the eye. This is one reason why multifocal diffractive lenses have a smaller light efficacy, and patients with such lenses implanted require proper illumination for tasks, that require detailed resolution, e.g., reading.

Another reason for potential postoperative optical problems is the fact that the images of both diffractive generated foci are always displayed on the retina. Therefore, another great amount of light is lost for vision in each of the defined distances. Furthermore, the overlap of the two images leads to a certain loss in contrast sensitivity.

Apodization

Apodization is a commonly used optical term, and the principle is used in many diffractive optic systems. It describes optical filtering for

Apodized Diffractive Intraocular Lens, Fig. 1 Appodized diffractive aspheric blue filtering single-piece intraocular lens. (ReSTOR, Alcon, Fort Worth, Texas, USA). One can see the central diffractive circular steps with decreasing distance from each other

enhancement of contrast sensitivity at expense of resolution. This is usually done by peripheral reduction of transmission. In case of multifocal diffractive IOL, it is performed by decreasing thickness of the circular zones from the center to the periphery to minimize optical phenomena (Fig. 1).

Cross-References

- ▶ Bifocal Lenses
- ▶ Contrast Sensitivity
- ▶ Light Adaptation
- ▶ Multifocal Intraocular Lens
- ▶ Multifocal Lenses
- ▶ Optic Disc (Optic Nerve Head)
- ▶ Refraction
- ▶ Wavefront Sensing

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Apraxia of Lid Opening

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Definition

Apraxia of lid opening (ALO) is a potentially disabling syndrome characterized by a non-paralytic difficulty in voluntary initiation of

the act of lid elevation after lid closure. Although called an apraxia, apraxia of lid opening is not a true apraxia (typically defined as a voluntary inability to perform a motor task to command). ALO may present with difficulty to open the eyes in one instance but then be normal in other instances. The pathophysiology of ALO is poorly understood, but the predominant proposed theory is thought to be related to an abnormality in the supranuclear control of voluntary elevation of the eyelid. The normal eyelid opening requires an activation of the levator palpebrae superioris muscle (LPS) and the concomitant inhibition of orbicularis oculi muscle (OO). Electromyographic (EMG) studies have revealed involuntary LPS inhibition and persistent contraction of pretarsal OO in some patients. Anatomically the LPS receives bilateral innervation from the central caudal subdivision of the oculomotor nucleus, and the OO muscles receive unilateral innervation from the facial nucleus. The cortex, rostral midbrain, and extrapyramidal motor systems also modulate and control LPS motor neuron activity, and any disturbances of these premotor structures may result in an abnormal inhibitor of LPS. ALO is frequently associated with benign essential blepharospasm (BEB) and has been variably reported in 7–55% of patients with blepharospasm. The peak age of onset is in the sixth and seventh decades of life, and it has been reported to be more common in women with female-to-male ratio of 2:1 with no racial differences.

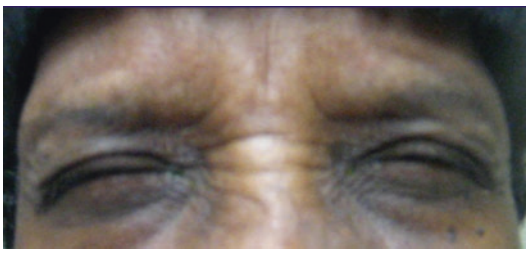
Etiology

Aside from its association with BEB, ALO has been described in nondominant hemisphere, medial frontal lobe, basal ganglia, and rostral brainstem lesions and in association with a variety of central nervous system (CNS) diseases such as progressive supranuclear palsy (PSP), Parkinson disease, other motor neuron diseases, idiopathic and secondary dystonias, Huntington chorea, hydrocephalus, choreoathetosis, and Shy-Drager syndrome. In addition, it has been reported in association with medication intoxication such as lithium intoxication, sulpiride, and 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP).

Clinical Presentation

ALO can present in isolation in healthy individuals or in patients with known neurodegenerative or neurologic disorders as above. ALO is a chronic disorder without cure; however, spontaneous improvements and remissions have been reported. Patients with ALO present with difficulty in opening the lids at will subsequent to voluntary or involuntary closure. See Fig. 1. Once the lids are opened, the LPS has normal tone and the patient usually then has no trouble keeping the lids opened. The lids usually open more easily during reflex blinking. In BEB patients, intermittent involuntary closure of the eyes may occur in the presence or absence of spasmodic contractions of the OO. In some instances attempting eye opening can result in a vigorous contraction of the frontalis muscle, backward thrusting of the head, and delay in lid closure.

Patients with ALO often adapt different "sensory tricks" and maneuvers to help with opening the eyes, such as manually lifting the lids, elevating their brows, massaging the lids, opening the mouth, and lightly touching or tapping the temporal region; however the physiology why these maneuvers help remains unknown. In general,



Apraxia of Lid Opening, Fig. 1 A patient with blepharospasm has concomitant apraxia of eyelid opening. Mechanical opening of the lids or use of an alleviating maneuver (e.g., sensory trick) can stop or reduce the spasm and allow the lids to open

the coordination of eyelid movement, pursuit eye movements, both horizontal and vertical saccades, and vestibulo-ocular reflex all are preserved. ALO is frequently confused with upper eyelid ptosis, though it usually occurs in the absence of levator weakness.

Diagnostics

The first step in the diagnosis depends on the exclusion of underlying diseases or medication intoxication that may be associated ALO. Neuroimaging studies using computed tomography (CT) scanning or magnetic resonance imaging (MRI) may help reveal whether a pathologic etiology is present. Studies showed using brain positron emission tomography (PET) has demonstrated glucose hypometabolism suggesting abnormal neuronal activity in the basal ganglia, the unilateral or bilateral medial frontal lobe, and the primary visual cortex. Other diagnostic tools have been used to demonstrate LPS and OO muscle activity during lid movements including electromyography (EMG). Neuropsychological testing may be considered to document the presence or absence of frontal lobe pathology.

Differential Diagnosis

1. Benign essential blepharospasm
2. Cerebral ptosis
3. Hemifacial spasm
4. Eyelid myokymia
5. Bell palsy
6. Facial nerve misdirection (synkinesis)
7. Spastic-paretic facial contracture
8. Drug side effect (antipsychotic, antiemetics, anorectics, nasal decongestants, levodopa)
9. Ophthalmic causes: conjunctivitis, keratitis, foreign body, allergy, keratoconjunctivitis sicca, and uveitis
10. Nonorganic lid closure

Therapy: Treat Any Underlying Etiology

Medical Management

The drugs that have been used in the management of ALO are:

1. Neuromuscular blockers such as botulinum toxin can treat blepharospasm and may improve ALO (Botox, Allergan, Inc., Irvine, CA)
2. Antiparkinsonian agents: dopamine agonists, e.g., carbidopa and levodopa (Sinemet) anticholinergic agents (e.g., trihexyphenidyl, benztropine (Cogentin))
3. Anticonvulsants (e.g., valproic acid (Depacon, Depakene, Stavzor))

Surgical Management

The procedures that have been used in the management of ALO are:

1. Frontalis suspension and myectomy
2. Levator palpebrae superioris (LPS) aponeurosis reinsertion

Cross-References

- ▶ Bell Palsy
- ▶ Benign Essential Blepharospasm: Orbital and Oculoplastic Considerations
- ▶ Eyelid Trauma

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Aptamer

► Antivascular Endothelial Growth Factor

Aqueous

► Aqueous Humor

Aqueous Humor

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Synonyms

Aqueous

Definition

The aqueous humor is a clear, colorless fluid that fills the anterior portion of the eye which is formed from plasma by the nonpigmented cells of the ciliary body.

Basic Characteristics

Aqueous humor has several functions including providing nutrition to and removing metabolic waste from the lens, trabecular meshwork, and cornea. It maintains intraocular pressure and has a role in the optical system of the eye by having the characteristics of being clear and colorless. It also has a role in paracrine signaling and immune responses.

Aqueous is an ultrafiltrate of plasma formed by the ciliary body; however, compared to plasma, aqueous is slightly hypertonic and acidic with a pH of 7.2 and contains much less protein and relatively less bicarbonate, calcium, and glucose. However, it contains much more ascorbate and relatively more hydrogen, chloride, and lactate. It also contains small amounts of amino acids, coagulation factors, growth factors, carbonic anhydrase, lysozyme, diamine oxidase, cAMP, catecholamines, steroid hormones, and hyaluronic acid. In the setting of inflammation or trauma, there is an increase in protein concentration in aqueous.

Aqueous is formed via three mechanisms. The first process, which accounts for most aqueous production, is active transport, a process which consumes energy and moves substances against an electrochemical gradient, independent of intraocular pressure. Next, ultrafiltration allows pressure-dependent movement of substrates along that pressure gradient. Finally, simple diffusion allows passive movement of ions across a membrane related to charge.

Aqueous humor is formed at a rate of 2–3 μl/min. Since the amount of aqueous in the anterior and posterior chambers is about 250 μl, aqueous turnover is about 1% turnover of volume per minute. Its formation varies diurnally and decreases during sleep and with age, injury, inflammation, and general anesthesia.

After production in the posterior chamber, aqueous flows through the pupil into the anterior chamber and then exits the eye through the trabecular meshwork or the uveoscleral pathway. The angle of the eye is a ringlike structure that lies where the cornea and iris meet. The trabecular meshwork is one of the circular structures that are located in the angle. The trabecular meshwork functions like a filter between the anterior chamber and Schlemm's canal. Once fluid passes from the anterior chamber into Schlemm's canal, it flows into the collector channels and then aqueous

veins. The main site of resistance in this pathway is the juxtacanalicular layer of the trabecular meshwork and the adjacent endothelial lining of Schlemm's canal. Fluid exiting the eye via the uveoscleral pathway passes through the ciliary muscle and sclera.

Since the mainstay of glaucoma treatment is lowering intraocular pressure, most medications to treat glaucoma lower pressure by one of two ways: decreasing aqueous production (beta-blockers, alpha-adrenergic agonists, carbonic anhydrase inhibitors) or increasing aqueous outflow (parasympathomimetic agents, prostaglandin analogs). Surgical procedures to treat glaucoma also target aqueous production and outflow. Aqueous reduction can be achieved by applying laser to the ciliary processes of the ciliary body which reduces production of aqueous by disrupting a portion of the function of the nonpigmented epithelial cells. The most commonly used surgical techniques to increase aqueous outflow are trabeculotomy, trabeculectomy, or a variety of commercially available implants which bypass the trabecular and uveoscleral outflow pathways, as well as a few other ways.

Cross-References

► Ciliary Body
► Intraocular Pressure

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Aqueous Misdirection

► Ciliary Block (Malignant) Glaucoma, Muscarinic Antagonists for

Aqueous Misdirection Syndrome

► Ciliary Block "Malignant" Glaucoma

Arachnoid Mater, Optic Nerve

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Synonyms

Arachnoid membrane

Definition

The arachnoid mater makes up one of three meningeal layers surrounding the optic nerve

and brain. From outermost to innermost, the layers are dura mater, arachnoid mater, and pia mater. The three layers around the optic nerve are collectively referred to as the optic nerve sheath. The arachnoid mater is made up of several layers of meningothelial cells, connected together by desmosomes, as well as a collagen bundle network. Beneath the arachnoid mater, there is a subarachnoid space, which holds cerebrospinal fluid (CSF). Arachnoid trabeculae traverse the subarachnoid space and insert themselves into the connective tissue of the pia mater. Blood vessels reach the optic nerve through the arachnoid trabeculae and travel along the optic nerve in the connective tissue of the pia mater. Once the optic nerve reaches the orbit, the meninges blend into the outer layer of the sclera. Increased intracranial pressure in the CSF can be transmitted to the optic nerve head along the optic nerve sheath meninges (i.e., papilledema). Tumors of the meninges can arise from or involve in the optic nerve sheath (i.e., optic nerve sheath meningioma). Infiltrative and inflammatory disease can also occur in the sheath primarily or extend from the intracranial meninges.

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Arachnoid Membrane

► Arachnoid Mater, Optic Nerve

Arc Welding, Occupational Light Injury and

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Synonyms

Flash burn; Phototoxic maculopathy; Welder's flash or arc eye; Welders maculopathy

Definition

Welding arcs emit radiation over a broad range of wavelengths – from 200 to 1,400 nm. This includes ultraviolet (UV) radiation (200–400 nm), visible light (400–700 nm), and infrared (IR) radiation (700–1,400 nm). The light emitted can cause injuries to various structures of the eye, mainly to the cornea.

The acute cornel damage from arc welding is photokeratitis. It is caused by UV rays, which irritate the superficial corneal epithelium, causing inhibition of mitosis, production of nuclear fragmentation, and loosening of the epithelial layer. An inflammatory response occurs, which includes edema and congestion of the conjunctiva and a stippling of the corneal epithelium. The first signs are foreign body sensation, photophobia, tearing, blepharospasm, and pain, occurring 6–12 h after the injury. The major finding on examination is superficial punctate keratitis (SPK), characterized by small pinpoint defects in the superficial corneal epithelium, which stain with fluorescein. If SPK is severe, it may be followed by total epithelial desquamation, with conjunctival chemosis, lacrimation, and blepharospasm. The goal of photokeratitis therapy is to treat the pain associated with damage to the corneal epithelium and to

prevent infection while the cornea heals. Usually the treatment includes topical antibiotics, topical cycloplegics, and oral analgesics. Reepithelialization usually occurs within 36–72 h, and long-term sequelae are rare. Chronic UV radiation exposure from arc welding is associated with a high prevalence and incidence of long-term changes in the outer segments of the eye, including pterygium, pingueculum, keratoconjunctivitis, and allergic conjunctivitis.

UV light (100–400 nm) is absorbed by the cornea and the lens, while visible light and IR light radiation (400–1,400 nm) penetrates the eye and absorbed by the retina and may cause thermal or photochemical damage. The type of retinal damage depends on wavelength, energy level, duration of exposure, and degree of pigmentation. Retinal damage induced by arc welding is referred to as phototoxic maculopathy. It is caused by a photochemical cascade of reactions which may release free radicals, hyperoxide anions, and hydrogen peroxide, which may react with the tissue and membranes to form aldehydes when these substances are not degraded promptly. Several retinal mechanisms are existing to prevent a phototoxic injury, including molecular detoxification, antioxidants, and lipofuscin deposits. Phototoxic retinal changes include damage to the outer retinal layers and to the retinal pigment epithelium (RPE). These changes are typically subtle and it is difficult to identify and document them clinically. Optical coherence tomography (OCT), multifocal electroretinography (ERG), and perimetry have been reported as effective methods for documenting the retinal layer changes with this type of injury. OCT revealed an interruption or defect of the inner/outer segment (IS/OS) and/or the RPE layer in various degrees. Most of these affected welders have a good corrected visual acuity. This finding suggests that subtle macular damages and visual acuity can be relative independent factors. In most cases, retinal injuries heal spontaneously without loss of vision. However, if there is a severe damage to the RPE or outer layers of the retina, it may lead to permanent, complete, or partial loss of central vision.

Arcuate Keratotomy

▶ Astigmatic Keratotomy

Arcus Juvenilis

▶ Corneal Arcus

Arcus Senilis

▶ Corneal Arcus

Arden Ratio

▶ Electrooculogram

Argon Laser Photocoagulation

▶ Argon Laser Therapy

Argon Laser Therapy

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Synonyms

Argon laser photocoagulation

Definition

Argon laser obtains its energy delivery in the ions of argon gas. It has an ability to produce tens of watts of continuous wave power in the region of blue (488 nm) and green (514.5 nm) wavelengths.

Selected tissues, such as retinal pigment epithelium (RPE), can be heated by thermal reaction, classified as photocoagulation, and induced by the argon laser. Because melanin in RPE cells absorbs wavelengths in the range of argon better than those in the range of other ions of noble gas, it is the preference for photocoagulation of the RPE. In addition, since the blue wavelength of argon can cause damage to inner retina, the green wavelength is more commonly used for photocoagulation of the neurosensory retina and RPE (L'Esperance 1989; Karlin 1995).

Argon laser photocoagulation was used in many major randomized controlled clinical trials that were landmarks and set the standards for treatment of common retinal vascular diseases.

Indication

The eyes with proliferative diabetic retinopathy (PDR) that have reached the high-risk stage should receive prompt treatment with argon panretinal photocoagulation (PRP). The high-risk PDR was defined in the Diabetic Retinopathy Study (DRS) and used commonly in clinical practice as neovascularization of the optic disk (NVD) larger than one-third disk area alone or any NVD or any neovascularization elsewhere (NVE) with vitreous hemorrhage (VH) (Royle et al. 2015).

However, the eyes with PDR that have not yet reached this stage may also have benefits from early PRP if the patients have type I diabetes, poor systemic controls, or difficulty in following up.

The eyes with clinically significant macular edema (CSME), defined as clinical observation of retinal thickening within the center of macula in the Early Treatment Diabetic Retinopathy Study (ETDRS), should receive argon focal laser photocoagulation of the macula. In the current era of optical coherent tomography (OCT), which allows better detection of diabetic macular edema than clinical examination, recent randomized controlled trials have demonstrated visual benefits of anti-vascular endothelial growth factor (anti-VEGF) agents over focal laser photocoagulation for treatment of center-involved diabetic macular edema (DME).

However, selected eyes with persistent DME that are not improved with anti-VEGF agents may be treated with focal laser photocoagulation. Selected eyes with DME, such as those with focal areas of thickening, may also receive the initial treatment with argon laser photocoagulation to those areas.

The eyes with central retinal vein occlusion (CVO) and the eyes with branch retinal vein occlusion (BVO) should receive PRP and quadratic scatter photocoagulation, respectively, only when rubeosis ($\geq$2 clock-hour of iris or any angle neovascularization), NVD, NVE, or neovascular glaucoma develops (Weingeist and Sneed 1992).

The eyes with extrafoveal choroidal neovascularization in neovascular age-related macular degeneration or other diseases may also be treated with argon focal laser photocoagulation.

The eyes with retinal breaks and rhegmatogenous retinal detachment are indicated for argon focal laser photocoagulation to create strong adhesion between the neurosensory retina and RPE.

Argon focal laser photocoagulation is also used for treating leakage points of long-standing or recurrent central serous chorioretinopathy. It may be used for treatment of various retinal vascular diseases, such as macular telangiectasia, retinal arterial macroaneurysms, and Coats' disease with variable results. Certain retinal or choroidal tumors may be treated with argon laser photocoagulation if the tumors contain pigment that absorbs the laser, such as choroidal melanoma (Weingeist and Sneed 1992).

Contraindication

Argon blue laser may not be used for photocoagulation in macular area. The macula may be damaged due to high absorption of this wavelength by xanthophyll pigment in this area (L'Esperance 1989; Karlin 1995).

Techniques and Principles

Energy of argon laser can be delivered to an eye via slit lamp, binocular indirect ophthalmoscope (BIO), or endolaser probe during vitrectomy.

The conventional slit-lamp delivery system requires contact lens for focusing laser beam on target tissues. There are two types of the contact lens: plano-concave and high plus. The former creates a virtual, upright, image with limited field of view; the latter creates a real, inverted, image with wider field and is more appropriate for PRP (Weingeist and Sneed 1992).

The binocular indirect ophthalmoscope (BIO) system has advantages in treating patients who are not able to sit at the slit lamp and treating retinal periphery with or without scleral indentation. This system is commonly used for photocoagulation of retinopathy of prematurity. Special care should be taken while performing BIO laser since its power may be variable with change in head position of the surgeon or the patient.

For conventional PRP, applying moderate intensity of 800–1,600 burns (500-μm spot size) in separated sessions is recommended. The laser burns with pulse durations from 0.1 to 0.2 s are placed one by one in a grid pattern outside the vascular arcades. Direct treatment on flat NVE on retinal surface is possible; however, elevated NVE should be treated with caution. PRP may regress NV in PDR and other retinal vascular diseases by improving oxygen flow to the retina from choroids through the photocoagulation scar and destruction of ischemic retina that produces VEGF.

Modified-ETDRS focal photocoagulation technique is currently recommended for treatment of DME. This technique requires 50 μm of burn size and 0.05–0.1 s of burn duration for both direct treatment on leaking microaneurysms and grid treatment on all areas of edema not associated with the microaneurysms. The burn intensity should be barely visible and change in color of microaneurysms is not required.

In current clinical practice, the treatment of retinal and choroidal diseases by argon laser has mostly been taken by frequency-doubled Nd:YAG laser which provides an output wavelength of 532 nm. The typical wavelength of 1,064 nm of the solid-state Nd:YAG laser is transformed by an arrangement of nonlinear potassium titanyl phosphate (KTP) crystal within the system. The system of this practically "green" Nd:YAG laser has overcome some limitations of argon laser system, such as requirement of special electrical hookup and plumbing attachment, while maintaining all the clinical properties of argon green laser photocoagulation (Karlin 1995).

Outcome

Argon laser PRP in high-risk PDR, according to the DRS, can decrease the incidence of severe visual loss by 50% or more. Argon focal laser photocoagulation for CSME, according to the ETDRS, can reduce moderate visual loss by 50% or more (Royle et al. 2015). The modified-ETDRS technique of focal treatment of center-involved DME shows similar results as the ETDRS.

Argon PRP can regress significant NV in CVO, according to Central Vein Occlusion Study (CVOS). However, prompt regression of the NV in response to PRP is more likely to occur in eyes that have not been treated previously. Prophylaxis PRP does not completely prevent the NV to occur in CVO. Argon quadratic scatter photocoagulation can decrease the risk of VH in BVO compared to eyes without the treatment, according to Branch Vein Occlusion Study (BVOS). However, similar to CVOS, photocoagulation before neovascularization develops is not beneficial.

Complications

Although less likely than other lasers with longer wavelengths, argon laser photocoagulation can also break Bruch's membrane and cause choroidal neovascularization. This may occur when very high power or very short burn duration is used. For example, argon endolaser photocoagulation in vitreoretinal surgery, which delivers high energy very close to the retina, may rupture Bruch's membrane and causes choroidal hemorrhage more frequently than the slit lamp system (Weingeist and Sneed 1992).

Inadvertent foveal photocoagulation is the worst and most feared complication of both focal laser treatment of the macula and PRP.

For PRP, potentially severe but avoidable complications are accidental photocoagulation of the posterior pole and contraction of the existing

fibrous tissue at the vascular arcade of PDR. To avoid this complication, laser burns should not be placed close to the fibrosis.

Very extensive PRP, such as applying more than 1,000 spots of too strong burns in a single session of treatment, can cause transient changes of choroids, such as choroidal detachment, myopic shift from anterior displacement of lens-iris diaphragm, and exudative retinal detachment. Secondary intraocular pressure rising can also occur. These transient changes may improve spontaneously within a few weeks after PRP.

PRP may cause macula edema or worsening of existing macular edema. It is recommended to treat macular edema before initiating PRP.

Mild and unavoidable side effects of PRP include peripheral and paracentral visual field loss. Scotopic visual impairment can occur due to damage to rod cells. Damage to short ciliary nerves is uncommon, but it may cause partial internal ophthalmoplegia.

Accidental coagulating anterior segment structures, such as iris, cornea, and lens, is possible when the laser beam is not focused properly on the retina or when there is an air bubble between the contact lens and cornea during the procedure. Poorly reactive pupil or decrease in accommodation is a side effect when the pupil is injured.

Cross-References

- ▶ Argon Laser Photocoagulation
- ▶ Diabetic macular edema
- ▶ Diabetic retinopathy
- ▶ Early Treatment Diabetic Retinopathy Study (ETDRS)
- ▶ Laser Focal Treatment

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Argyll Robertson Pupil

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Definition

The Argyll Robertson (AR) pupil refers to small, irregularly shaped pupils bilaterally that can accommodate to a near stimulus but do not react well to direct light stimulus. Historically, this finding indicates neurosyphilis but other conditions can produce AR pupils.

Differential Diagnosis

AR pupil primarily affects patients suffering from neurosyphilis but can also be associated with diabetes, multiple sclerosis, Wernicke encephalopathy, Charcot-Marie-Tooth disease, herpes zoster, Lyme disease, sarcoidosis,

midbrain lesions, Dejerine-Sottas hypertrophic neuritis, and von Economo encephalitis.

Pathogenesis

The AR pupil is due to a lesion in the midbrain involving the connections to the Edinger-Westphal nucleus for the pupil which are rostral within the periaqueductal gray matter. The rostral location of the midbrain pathology allowing for disrupts the pupillary light reflex but spares the accommodation fibers. More extensive caudal lesions would likely affect both the pupillary and accommodation pathways.

Clinical

The AR pupil is characterized by small (miotic) pupils which are irregular, do not respond to light, and then become even more miotic (pinpoint) to near stimulus. Serologic testing for syphilis is recommended including non-Treponemal (e.g., rapid plasma reagin (RPR) and Venereal Disease Research Laboratory (VDRL)) testing as well as Treponemal testing (e.g., FTA-Abs or MHA-TP). Neuroimaging and lumbar puncture with cerebrospinal fluid analysis for neurosyphilis testing is generally also recommended.

Treatment

Treatment is generally directed against the cause for the AR pupils (e.g., intravenous penicillin therapy for neurosyphilis).

Prognosis

The prognosis depends upon the etiology, duration of findings, and efficacy of treatment of the underlying etiology.

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Aristocort Acetonide

▶ Intravitreal Triamcinolone

ARMD

▶ Age-Related Macular Degeneration

Arterial Dissection

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Synonyms

Arterial tear

Definition

An arterial dissection is defined as a tear in an arterial wall. The tear involves the intima of the

artery, creating a false lumen and allowing blood to enter the intima and media space of the artery. Most dissections with ophthalmic symptoms occur in the cervicocranial arteries, which is the internal carotid artery and/or the vertebral artery. The dissection is often extracranial but can extend or involved the intracranial arteries. Cervicocranial arterial dissections usually occur at the sites where the artery is mobile, and not fixed to the dura mater or to other arteries, thus making extracranial arteries the most common locations for dissections. They can be caused by trauma or can be spontaneous. Most cases are traumatic, but the trauma necessary for a cervical dissection can be as minimal as a quick turn or minor manipulation of the neck. Blood may pool inside the false lumen and cause ischemia due to compression. The blood may also clot in the false lumen and be released into the true lumen, causing a thromboembolic stroke.

Epidemiology

Cervical artery dissection has an annual incidence of 2.6–3.0 per 100,000. These arterial dissections account for a small percentage of all ischemic strokes, roughly about 2%, but account for 10–25% of strokes in young and middle-aged patients.

History

The earliest documentation of an arterial dissection is from the year 1760, when King George II of England died from a fatal cardiac tamponade due to an aortic dissection that had ruptured into the pericardial sac. The term "aortic dissection" was established in 1802, but the term "dissecting aneurysm" was favored at the time. In Houston, in the 1950s, Dr. DeBakey and his team performed the first successful surgical repair of a dissecting aortic aneurysm.

Clinical Features

Most patients with cervicocranial dissections will experience a headache and may have sharp pain in the jaw, neck, or face. The ophthalmic symptoms that usually occur are a painful ipsilateral Horner syndrome, transient or permanent vision loss from thromboembolic retinal arterial disease, and scintillations or flashing lights. One study found that 52% of patients with cervicocranial dissections presented with ophthalmic symptoms (Biousse et al. 1998). The sympathetic fibers travelling along the internal carotid artery are disturbed and lead to a partial or complete ipsilesional Horner syndrome (ptosis and miosis). Anhidrosis is not typically seen because the innervation to the sweat glands travels along the external carotid artery. Many patients with cervical dissections will present with symptoms very similar to a migraine, mainly headache and scintillations. The presentation of an acute Horner syndrome with ipsilateral head or neck pain is characteristic of cervical dissection and should be considered as suggestive of an internal carotid artery dissection until proven otherwise.

Tests

The diagnosis of a cervical dissection can be made noninvasively through imaging (e.g., ultrasound, magnetic resonance imaging (MRI), magnetic resonance angiogram (MRA), or computed tomography (CT)). MRI with MRA is typically performed for the diagnosis of a cervicocranial arterial dissection. T1-weighted MRI of the head and neck is highly sensitive and specific for diagnosing cervicocranial dissections in combination with MRAs. CT and CT angiography (CTA) of the head and neck however have also been proven effective for diagnosing a dissection and are a faster study than MRI/MRA. There is some radiation exposure with CT/CTA, but CT may be necessary for patients with MRI contraindications or in those who require an emergent study. Any patient who presents with an unexplained Horner syndrome in conjunction with neck or head pain should be evaluated for a possible cervicocranial dissection.

Differential Diagnosis

The differential diagnosis of arterial dissection includes migraine, atherosclerosis, subarachnoid

hemorrhage, ischemic or hemorrhagic stroke, cervical strain, cervical fracture, and giant cell arteritis

Etiology

The etiology of cervical artery dissections is not well understood. It is believed that most patients who experience a cervical artery dissection have an underlying vessel wall weakness and then undergo an environmental trigger (i.e., trauma) to cause their dissection. People with acquired irregularities of the vessel walls, such as connective tissue disorders (e.g., Marfan syndrome, Ehlers-Danlos syndrome), fibromuscular dysplasia, and cystic medial necrosis are more likely to experience arterial dissections. The main environmental risk factor that has been studied and found to be consistently involved in cervical artery dissections is trauma. The trauma can be minor, such as a violent cough or quick turn of the neck, or major, such as a motor vehicle accident.

Treatment

In the acute phase of cervicocranial artery dissection treatment, anticoagulant or antiplatelet therapy is recommended to prevent any further ischemic events from occurring. There has not been a sufficiently powered randomized controlled clinical trial for evaluating the efficacy of treatment, and thus therapeutic decisions are made on a case-by-case and institutional basis. Anticoagulation may be more favorable when there is severe stenosis or occlusion with a large risk of embolization. Antiplatelet therapy is favored if there is a contraindication to anticoagulation or if the dissection is associated with a large infarct, for theoretic risks of hemorrhagic conversion. For long-term therapy, anticoagulants are usually given for a period of 6 months. The duration of antiplatelet therapy has not been established but can be reassessed with follow-up imaging. If the cervical dissection presents with an ischemic stroke, thrombolytic therapy should not be withheld and should be administered as protocol for ischemic strokes.

Cross-References

▶ Diffusion-Weighted Magnetic Resonance Imaging

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Arterial Tear

▶ Arterial Dissection

Arteriohepatic Dysplasia (AHD)

▶ Arteriohepatic Dysplasia (Alagille Syndrome), Retinal Degeneration

Arteriohepatic Dysplasia (Alagille Syndrome), Retinal Degeneration

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Synonyms

Alagille-Watson syndrome (AWS); Arteriohepatic dysplasia (AHD); Cholestasis with peripheral pulmonary stenosis; Syndromatic hepatic ductular hypoplasia

Definition

Alagille syndrome (ALGS; OMIM #118450) is an autosomal dominant inherited multisystem disease. The syndrome affects primarily the liver, heart, eyes, face, and skeleton. The penetrance is highly variable within and between different affected families. The syndrome was first described by Alagille et al. in 1969, and additional cases were reported by Watson and Miller in 1973, and again by Alagille et al. in 1975, leading to the establishment of diagnostic criteria. Prevalence of ALGS is estimated to be in the range of 1:30,000–1:70,000 live births taking into account the variability and the low penetrance of the disease. The most common characteristic manifestations of the disease are juvenile cholestasis combined with bile duct paucity on liver biopsy; congenital cardiac defects, primarily involving the pulmonary arteries; posterior embryotoxon in the eyes; typical facial features; and butterfly vertebrae.

Etiology

ALGS is classified into two subtypes based on the mutated gene. The majority of cases (about 97%) are classified as ALGS type 1 which is associated with haploinsufficiency of the Jagged-1 gene (*JAG1*) on chromosome 20p12 (encoding JAGGED1 protein). Approximately 60% of the mutations are *de novo*. Less than 1% of the cases are caused by mutations in the *NOTCH2* gene on chromosome 1p12, encoding the NOTCH2 transmembrane protein, causing ALGS type 2 (OMIM #610205). Both genes are components of the notch signaling pathway which is known to take part in normal angiogenesis. No consistent phenotype-genotype correlation was reported.

Clinical Presentation

ALGS involves multiple organs including the liver, heart, eye, skeleton, face, kidneys, vessels, pancreas, growth, and learning abilities (Table 1).

Ocular defects affect mainly the anterior segment of the eye, but defects in the retina and optic disc are also common.

Arteriohepatic Dysplasia (Alagille Syndrome), Retinal Degeneration, Table 1 Classic criteria, based on five body systems, for a diagnosis of Alagille syndrome (Adapted from Turnpenny and Ellard (2012))

System/problem	Description
Liver/cholestasis	Usually presenting as jaundice with conjugated hyperbilirubinemia in the neonatal period, often with pale stools
Dysmorphic facies	Broad forehead, deep-set eyes, sometimes with upslanting palpebral fissures, prominent ears, straight nose with bulbous tip, and pointed chin giving the face a somewhat triangular appearance
Congenital heart disease	Most frequently peripheral pulmonary artery stenosis, but also pulmonary atresia, atrial septal defect (ASD), ventricular septal defect (VSD), and tetralogy of Fallot (TOF)
Axial skeleton/ vertebral anomalies	"Butterfly" vertebrae may be seen on an anteroposterior radiograph and occasionally hemivertebrae, fusion of adjacent vertebrae, and spina bifida occulta
Eye/posterior embryotoxon	Anterior chamber defects, most commonly posterior embryotoxon, which is prominence of Schwalbe's ring at the junction of the iris and cornea

The largest series of patients with Alagille syndrome was published by Hingorani et al. (1999) and reported 22 patients with ALGS and their parents; the characteristic ocular pathologies were summarized. The most prevalent ophthalmic defects were posterior embryotoxon (95%), iris abnormalities (45%), diffuse fundus hypopigmentation (57%), speckling of the retinal pigment epithelium (33%), and optic disc anomalies (76%). No serious functional effect and no relation to nutrient vitamins A and E were demonstrated.

- **Posterior embryotoxon** (**PE**): The hallmark ophthalmic feature associated with ALGS is posterior embryotoxon. It is defined as central dislocation and thickening of the border of the Schwalbe's line of the cornea, at the junction between the corneal endothelium and the trabecular meshwork. This finding was associated

with other pathologies including Axenfeld-Rieger syndrome, Peter's anomaly, and DiGeorge syndrome, and it manifests in 8–15% of the normal population. PE can be detected by routine slit-lamp examination and usually it does not affect the visual function.

- **Iris anomalies**: Hingorani and colleagues described some iris abnormality in 10 out of 22 patients (45%) with ALGS including hypoplastic anterior iris stroma, corectopia, and radial strands/cords. Axenfeld anomaly and Rieger anomaly, as separate entities or combined as Axenfeld-Rieger syndrome, are common findings in ALGS. Axenfeld anomaly was described in 1920 as a prominent circular gray-white line in the posterior surface of the cornea (Schwalbe's line) with iris strands. When it is accompanied by glaucoma, it is called Axenfeld syndrome. Rieger described in 1935 patients with similar findings with anomalies of the iris such as iris atrophy or corectopia. When these findings are associated with facial or dental anomalies, it is called Rieger syndrome. As these phenotypes overlap, the term Axenfeld-Rieger syndrome is often used. Axenfeld-Rieger syndrome can present as isolate ocular finding or associated with other ocular defects (sclerocornea, developmental glaucoma, persistent pupillary membrane, microphthalmos, and iris coloboma).
- **Diffuse fundus hypopigmentations and maculopathy**: Fundus defects were found in 90% of the patients examined by Hingorani and colleagues (1999); such defects included diffuse RPE hypopigmentation in 57% and speckling of the RPE in 33%. Both features were commonly detected in the mid-peripheral and peripheral zones. More recently, chorioretinal atrophy with punched out lesions encroaching on the posterior pole and subsequently causing visual acuity decrease in patients with ALGS was described (Makino et al. 2012).
- **Optic nerve head (ONH) drusen**: El-Koofy and colleagues (2011) examined 13 patients with ALGS and 19 patients with neonatal hepatitis and reported optic nerve head drusen in 91% of the ALGS patients compared to only 5.3% of patients with neonatal hepatitis making ONH drusen the most prevalent finding in ALGS patients.

  ONH drusen were demonstrated in at least one eye in 95% and bilaterally in 80% of patients with ALGS. Clinically, it was demonstrated in at least one eye in 90% of cases and bilaterally in 50% of ALGS patients. In contrast, these findings were not found in any of the eight non-ALGS-related cholestasis control patients. The incidence of ONH drusen in the general population is 0.3–2% (Nischal et al. 1996).
- **Optic disc edema**: Few cases with ALGS were reported to have idiopathic elevated intracranial hypertension with optic disc edema as a consequence. These patients had also the typical finding associated with ALGS, posterior embryotoxon (Mouzaki et al. 2010).
- **Myelinated nerve fiber layer**: Bilateral myelinated nerve fiber layer was also described in one case with ALGS (Voykov et al. 2009).
- **Miscellaneous ocular abnormalities**: Additional rare abnormalities were found in patients with ALGS including optic disc pit, serous macular detachment, and xerophthalmia. In that context, it should be noted that many of the associations of such findings with ALGS are based on case reports or small case series. Such associations might be incidental and further research is needed to establish their connection to ALGS.

Diagnosis

The diagnosis of ALGS is primarily based on clinical features. The following tests should be performed to support the clinical impression:

- Blood tests: for liver and kidney functions
- Urinalysis: to evaluate the kidney function and the elevated bilirubin levels
- X-ray: to look for butterfly vertebra and skeletal defects
- Abdominal ultrasound: to demonstrate enlarged liver and to rule out other causes for jaundice
- Cardiology exam: including physical exam by a cardiologist and echocardiography test for congenital cardiac abnormalities

- Slit-lamp exam: for ocular abnormalities including fundoscopy with pupil dilation
- Genetic tests: genotyping to identify mutations in the causative genes

Due to the variable expressivity and penetrance of the disease, it was suggested that three out of the five criteria in Table 1 should be diagnosed in an affected subject.

Alternatively, a diagnosis can be made in a subject who does not meet the classical criteria but harbors a mutation in either *JAG1* or *NOTCH2* genes.

Prognosis

Ocular abnormalities in ALGS are usually not associated with reduced visual functions unless complicated with secondary pathologies such as glaucoma or corneal insufficiency. The major morbidity and mortality of the syndrome are related to non-ocular multi-organ defects such as cardiovascular and hepatic diseases. Mortality of approximately 10% was reported among ALGS patients due to liver, cardiac, and vascular diseases.

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Arteriovenous Malformations (AVMs)

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Synonyms

AVM

Definition

An arteriovenous malformation (AVM) is a vascular lesion that directly connects the arterial and venous circulations without an intervening capillary bed, and AVMs can occur most anywhere in the body including cerebral AVMs. AVMs are being increasingly documented and can cause several neurological symptoms and even death.

Epidemiology

The overall incidence and prevalence of cranial AVMs is not well known, but has been estimated by autopsy and limited population-based studies.

Autopsy data shows that there is a frequency of detection of AVMs in about 4.3% of the population. Population-based studies report a detection rate of 1/100,000 adults per year and a prevalence of 18/100,000 adults/year (Scottish population-based registry). A population-based study in Minnesota found a detection rate of 1.1/100,000 adults and 2.1/100,000 adults when autopsy cases were included. Cerebral AVMs underlie 1–2% of all strokes and ~9% of all subarachnoid hemorrhages.

History

AVMs have been recognized since the ancient Egyptians in 1500 BC, and they were known to both the Roman and the Arab worlds. It was first described in Western medicine in 1757, but the first clinical diagnosis of an AVM has been attributed to Steinheil who diagnosed it in 1895. Operative interventions have been tried and modified since 1908. Cerebral angiography was developed in 1927 and has revolutionized the diagnosis and treatment of cerebral AVMs. The methods of treatment continue to evolve, including multimodal therapy (e.g., radiation therapy, interventional radiology, and surgery), and treatment should be individualized and with multidisciplinary input.

Clinical Features

Most cerebral AVMs are asymptomatic and are usually diagnosed before the age of 40 years. About 50% of patients with cerebral AVMs present with intracranial hemorrhage. The hemorrhage can be intracerebral (most common), subarachnoid, or intraventricular. Another 20–25% of patients with cerebral AVMs present with seizures; the seizures may be generalized or focal but are more often focal. Other presentations include headache, seen in 15% of patients, neurological deficits seen in 5% of patients, and pulsatile tinnitus. The headaches of cerebral AVMs have not been found to have any particular pattern, but may sometimes be accompanied by visual symptoms, such as blackouts. This is thought to be due to ischemia or change in flow of the occipital cortex. AVMs carry a 2–3% risk of hemorrhage per year, with mortality from the first hemorrhage lying between 10 and 30%. After the first hemorrhage, the risk of recurrence for the first year is about 6% and then drops back to baseline rate.

Tests

AVMs can be diagnosed through several different imaging studies, including computed tomography (CT), angiography (CTA), magnetic resonance imaging (MRI), and angiography (MRA). Standard digital subtraction catheter angiography is the gold standard for defining AVM anatomy and in treatment planning. CT scans may be done with or without contrast; although a CT scan without contrast has a very low sensitivity for AVM, a noncontrast CT may be useful to define intracranial hemorrhage. A contrast CTA or MRA might be diagnostic for an underlying AVM. MRI scans may also be done and are very sensitive; they also provide valuable information regarding localization of the lesion. In the presence of an AVM, a standard catheter digital subtraction angiogram is still generally needed to get a proper visualization of the AVM lesion and its anatomy.

Differential Diagnosis

Aneurysm, capillary telangiectasia, cavernous angioma, venous malformations

Etiology

AVMs are considered sporadic congenital vascular lesions, and their natural history and pathogenesis are poorly understood and variable. There are some associations between AVMs and hereditary diseases, such as hereditary hemorrhagic telangiectasia, an autosomal dominant disease associated with both pulmonary and cerebral AVMs. Although there are a few candidates, a gene has not been located as causing or predisposing to AVMs.

Treatment

There are four established treatments for cerebral AVMs; they include expectant monitoring,

microsurgery, endovascular embolization, and radiosurgery. Microsurgery has been the gold standard for treatment due to its immediate and complete obliteration of the AVMs. The Spetzler-Martin grading scale helps categorize the severity of the lesion as well as predict morbidity and mortality depending on nidus size and location and deep venous drainage. Endovascular embolization involves using microcatheters to navigate inside intracranial vessels and embolize the AVMs. Embolization can be performed with solid or liquid agents. Solid agents include fibers, microcoils, and microballoons, while liquid agents include cyanoacrylate monomers and polymer solutions. Embolization is usually done presurgically in very large malformations or before radiosurgery to reduce nidus size. Embolization can also be done as a palliative measurement to reduce flow size without removing the malformation in order to diminish symptoms. Lastly, radiosurgery irradiates the vessels of the malformation, causing the obliteration of the lumen and preventing rupture and hemorrhage. All three of these treatments have proven successful in treating cerebral AVMs.

Cross-References

▶ Retinae (Retinal Angiomatosis, von Hippel Syndrome/Disease)

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Arteritic AION

▶ Arteritic Anterior Ischemic Optic Neuropathy

Arteritic Anterior Ischemic Optic Neuropathy

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Synonyms

Arteritic AION

Definition

Arteritic anterior ischemic optic neuropathy (A-AION) is an ischemic disorder of the optic nerve that affects the anterior portion or head of the optic nerve due to vasculitis from giant-cell arteritis (GCA).

Etiology

A-AION specifically affects the anterior optic nerve head due to ischemia from the posterior ciliary arteries. Although A-AION is typically due to GCA, other vasculitic causes of AION

might include infection (e.g., herpes zoster vasculitis) or immune-mediated and inflammatory disorders (e.g., Crohn disease, rheumatoid arthritis, Behcet disease, anti-neutrophilic cytoplasmic antibody (ANCA) vasculitis, and systemic lupus erythematosus).

Clinical Presentation

Most patients with A-AION present with a sudden onset of visual loss, although in up to 30% of patients, transient monocular symptoms may precede vision loss. The visual loss in A-AION is variable but can range from 20/20 to no light perception vision, and severe visual loss is seen in over half of patients. Patients with GCA may have other systemic symptoms including jaw claudication; palpable, tender, or pulseless temporal artery; joint or muscle pains or myalgias (polymyalgia rheumatica); ear pain; headache; fatigue; fever; and chills.

Diagnostics

In addition to the visual acuity and/or visual field loss, patients with A-AION may have a relative afferent pupillary defect (RAPD) in unilateral or bilateral but asymmetric cases. The optic disk may show edema or in severe cases of A-AION, the disk may appear "chalky white" (i.e., pallid edema). In contrast to the non-arteritic form of AION (NAION), the after resolution of the disk edema, the optic disk may appear pale with an excavated glaucomatous-appearing optic cup. A-AION may be associated with concomitant cilioretinal artery, choroidal, retinal (cotton wool patches), or retinal artery ischemia. Fundus fluorescein angiography (FFA) might show impaired choroidal circulation in A-AION. Laboratory tests for GCA might reveal an elevated erythrocyte sedimentation rate (ESR), elevated platelet counts, or high levels of C-reactive protein (CRP). Temporal artery biopsy (TAB) is the gold standard however for definitively diagnosing GCA in patients with A-AION.

Differential Diagnosis

Non-arteritic anterior ischemic optic neuropathy (NAION), infectious optic neuropathy, inflammatory optic neuropathy, or infiltrative optic neuropathy.

Prophylaxis

GCA is considered the most common cause of A-AION. Patients diagnosed with GCA should be treated expediently with corticosteroids to prevent the development of A-AION in the fellow eye.

Therapy

A-AION is considered an ophthalmological emergency due to the rapid onset of vision loss. Currently, steroid administration is the mainstay treatment option. High doses of corticosteroids (oral or intravenous) can be used to reduce the risk of fellow eye visual loss in patients that have developed GCA and may prevent worsening unilateral or bilateral visual loss. Although steroid treatment may slow the progression of vision loss and protect the contralateral eye, only a small percentage of patients that have developed A-AION experience improvement in visual acuity.

Prognosis

A-AION often begins unilaterally but may occur simultaneously or progress to bilateral loss within days or weeks in untreated patients. Treatment with corticosteroids can prevent this progression to the fellow eye in unilateral cases but in most cases, loss of vision is irreversible once it commences.

Epidemiology

GCA and A-AION are seen in older patients (i.e., over the age of 50) with an incidence of 20 per 100,000 persons above the age of 50. The average age for diagnosis is 73 years old. Females are twice as likely as males to develop GCA and are thus also twice as likely to develop A-AION.

Cross-References

- ▶ Corticosteroids
- ▶ Giant Cell Arteritis
- ▶ Nonarteritic Anterior Ischemic Optic Neuropathy

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Arteritic Ischemic Optic Neuropathy

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Synonyms

Giant cell arteritis; Horton's arteritis; Temporal arteritis

Definition

Arteritic anterior ischemic optic neuropathy (A-AION) is the most important ophthalmologic manifestation of a systemic vasculitis commonly known as giant cell arteritis (GCA). GCA is a large- and medium-sized granulomatous arteritis that characteristically involves the extracranial branches of the carotid arteries, especially the temporal artery, but has a predilection for causing visual loss from involvement of the blood supply to the eye. GCA is the most common primary vasculitis among the older population. Early diagnosis and treatment of A-AION is critical since if untreated it may lead to bilateral blindness.

Etiology

GCA is an idiopathic chronic inflammatory disorder affecting medium- and large-sized arteries. Familial predominance, conjugal cases, and an association with the HLA-DR4 haplotype have been reported. Some authors have hypothesized that GCA might be infectious in origin (e.g., *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Burkholderia*, and parvovirus B19). Some immunological research has demonstrated an antigen-driven disease with local T-cell and macrophage activation in the vessel wall. The initial process may be a foreign body giant cell attack on calcified internal elastic membrane and on calcified atrophic parts of the aortic media.

Histopathology shows the presence of granulomatous vasculitis and thrombosis of the short posterior ciliary vessels in addition to variable involvement of the superficial temporal, ophthalmic, central retinal, and choroidal arteries. Ischemic necrosis is observed in the laminar and retrolaminar portions of the optic nerve producing A-AION and sometimes posterior ION (PION).

Clinical Presentation

The systemic symptoms and signs of GCA may appear subacutely or chronically (e.g., headache, fever, polymyalgia rheumatica, weight loss), but

the visual loss typically presents acutely in one or both eyes. Anterior ischemic optic neuropathy (AION) is the most common ophthalmological presentation of GCA. However, other presentations can include posterior ischemic optic neuropathy, central retinal artery occlusion, cilioretinal artery occlusion, amaurosis fugax, eye pain, diplopia, and ocular muscle paresis. Visual ischemic complications are found in up to 25% of patients with GCA, and unfortunately irreversible visual loss is found in 1–15% of patients. A history of amaurosis fugax, jaw claudication, cerebrovascular accident, absence of anemia, and a higher platelet count have been associated with an increased risk for permanent visual loss in one study.

The vision loss in A-AION is typically severe and may be as poor as 20/200 or worse in up to 60% of patients. Less severe visual loss may also occur in GCA however and patients may have no visual complaints at onset. Optic disc edema is often more pale and swollen at onset (i.e., pallid edema) in comparison to the non-arteritic form of anterior ischemic optic neuropathy (NA-AION) where the disc is typically hyperemic and shows non-pallid sector or diffuse disc edema. No optic disc edema is seen in the posterior form of ION (PION) and is a red flag for GCA in the elderly patient (visual loss, RAPD, and normal fundus). Cotton wool spots may also be a presenting finding in GCA. Choroidal ischemia may produce visual loss and may manifest as peripapillary pallor with or without optic disc edema. This choroidal-level ischemia might only be visualized on fluorescein angiography.

Constitutional symptoms in GCA are common (e.g., anorexia, fatigue, weight loss, fever), and many patients have polymyalgia rheumatica (proximal hip and shoulder girdle joint pain and morning stiffness). A new onset of or a new type of headache in elderly patients is a worrisome and common presenting symptom of GCA. Some patients experience carotidynia, and the pain of GCA may involve the head, scalp, face, neck, ear, tongue, or eye. The superficial temporal arteries may be thickened, nodular, tender, and erythematous, and temporal artery pulses may be decreased or absent. Jaw claudication is a less frequent and thus less sensitive but highly specific symptom of GCA (although it can also present in various other conditions including atherosclerosis, amyloidosis, and other vasculitis). Claudication of the tongue or necrosis of the tongue and scalp is less common but also highly suggestive signs of GCA.

GCA has been reported to cause other systemic and neurologic manifestations. Both the central and peripheral nervous system can be involved, resulting in transient ischemic attacks, strokes, dementia, spinal cord infarction, mononeuropathies, polyneuropathies, and subarachnoid hemorrhage. Thoracic and abdominal aortic aneurysms and dissection can also be seen in GCA. Intestinal infarction, coronary ischemia, pulmonary artery thrombosis, intra-alveolar hemorrhage, cough, sore throat, hoarseness, peripheral arthritis, hematuria, renal failure, and secondary amyloidosis are less common findings in GCA.

Diagnostics

The clinical presentation of A-AION is similar to that of NAION. Several red flags should raise suspicion for GCA (i.e., A-AION) however including (1) presence of systemic symptoms of GCA in a patient with AION (e.g., headache, jaw claudication, scalp tenderness, etc.); (2) episodes of transient visual loss (30%) or transient diplopia (5–10%) before A-AION presentation which would not be expected to occur in NAION; (3) peripapillary, retinal, or choroidal ischemia; (4) severe visual loss (e.g., light perception or no light perception vision); (5) bilateral simultaneous or rapidly sequential disease (if untreated, A-AION becomes bilateral in up to 95% of cases within days to weeks); (6) the affected swollen disc which is acutely pale and swollen (i.e., pallid edema) or appears normal despite RAPD and visual loss (i.e., posterior ION); and (7) the lack of the structural small, crowded, “disc at risk” for

NAION which may be absent in the contralateral eye of A-AION.

The work-up for A-AION is usually aided by laboratory evaluation. An elevated erythrocyte sedimentation rate (ESR) may be present. An ESR greater than 40 mm/h is seen in at least 77% of active untreated disease. However, the ESR is a nonspecific marker, and it can be present in a variety of inflammatory, infectious, and neoplastic disorders. Unfortunately, the ESR may be normal in 7–10% of GCA patients. A C-reactive protein in conjunction with the ESR may have a higher sensitivity (97%) and specificity (78%) for GCA. Normochromic, normocytic anemia and a reactive thrombocytosis may also be found in GCA.

The gold standard for the diagnosis of GCA is a temporal artery biopsy (TAB). The TAB typically demonstrates a vasculitis characterized by a predominance of mononuclear infiltrates or granulomas, usually with multinucleated giant cells. A normal TAB however does not exclude GCA since skip lesions can occur especially in small TAB specimens. Long specimens (>20 mm) may be more likely to yield a positive result. Unilateral temporal artery biopsy may be sufficient to exclude the diagnosis of GCA in patients with low clinical suspicion and has a sensitivity of about 96%. However, a contralateral biopsy should be considered in patients with high clinical suspicion to eliminate the remaining 4% false-negative rate. Some rare patients despite negative bilateral TAB might still need to be empirically treated if the clinical suspicion remains high for GCA.

Differential Diagnosis

Differential diagnosis of GCA includes:

1. Other medium/large vessel vasculitides: Takayasu, granulomatosis with polyangiitis (formerly Wegener granulomatosis), polyarteritis nodosa
2. Primary central nervous system (primary angiitis of CNS)
3. Trigeminal neuralgia
4. Sinus, dental disease, otological disease

Differential diagnosis of A-AION includes:

1. Non-arteritis anterior ischemic optic neuropathy
2. Optic neuritis
3. Other optic neuropathies: infection, inflammatory, genetic, neoplasm, compressive, toxic/metabolic, trauma

Prophylaxis

Non-applicable. Adequate and early high-dose steroid treatment might prevent first or fellow eye-related visual loss however in GCA.

Therapy

The initial treatment of choice for GCA is corticosteroids. The usual initial oral dose is 1–1.5 mg/kg of prednisone per day or its equivalent, and the response of systemic symptoms and elevated acute phase reactants (e.g., ESR and CRP) is generally rapid. Gradual and slow tapering after the initial high prednisone dose for 1–2 months based upon symptoms and lab testing is recommended. Typically, lower-maintenance doses or even a complete taper can be achieved after 12–18 months of treatment, but some patients require longer (e.g., 2–3 years) or even lifelong treatment. Flare-ups and relapses based upon symptoms and blood work usually respond to an increase in steroid dose to the last tolerated and effective dose, but there is significant variability in the response of the disease to steroids. Relapses may be more common during the first 18 months of treatment and the first week after suspension of steroid treatment. Although intravenous (IV) steroids may be considered (especially in patients with visual loss from A-AION or central retinal artery occlusion (CRAO)), there has been no head-to-

head direct comparison of oral versus IV to prove greater efficacy. Nevertheless, we consider IV steroids in GCA for patients who are monocular, who have transient visual loss episodes and severe or bilateral visual loss, or who are still symptomatic despite oral steroids at conventional doses.

A strong initial systemic inflammatory response may be associated with a more prolonged steroid course. Visual loss due to GCA treated with steroids improves only in a few patients. There is a better chance of improvement with early diagnosis and treatment. In suspected cases of GCA, it is reasonable to begin steroid treatment before biopsy results are available.

Prognosis

Corticosteroids can usually be reduced and discontinued in the majority of patients, but the course and duration of steroid treatment is quite variable from patient to patient. Some patients have a more chronic disease and may require chronic low doses of steroids for a number of years or even lifelong therapy. Permanent partial or complete visual loss has been found in 15–20% of patients, and steroids rarely restore any degree of visual loss in affected eyes. The new onset of visual loss in contralateral eyes is unusual once appropriate high-dose steroid treatment has been initiated. The mortality of treated patients with GCA does not seem to be increased compared with controls, but death may be due to cardiovascular disease, steroid therapy, or other complications of systemic vasculitis (e.g., aortitis).

Epidemiology

The most important risk factor for A-AION is older age. GCA occurs predominantly in white women older than 65 years of age; A-AION has a mean age of 70 years. It has an annual incidence of two per 10,000 persons. Diagnosis is more common in the northern latitudes; the highest incidences have been described in Scandinavian countries and North American population.

Cross-References

▶ Nonarteritic Anterior Ischemic Optic Neuropathy

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Arteritic PION (A-PION)

▶ Posterior Ischemic Optic Neuropathy

Artifactual Illness

▶ Munchausen Syndrome

Artificial Cornea

▶ Keratoprosthesis

Artificial Iris Implant

▶ Iris Prosthesis

Artisan Iris-Supported Phakic Intraocular Lens

▶ Verisyse Iris-Supported Phakic Intraocular Lens

Artisan Lens

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Synonyms

Iris-fixated phakic intraocular lens; Verisyse iris-supported phakic intraocular lens

Definition

A phakic IOL that is enclavated on the iris with specially designed "iris-claw" haptics.

Epidemiology

Before introduction of the lastest phakic IOL model (AcrySof), the iris-supported phakic IOL models (Artisan/Verisyse and Artiflex/Veriflex) were the most frequently implanted anterior chamber phakic IOLs (Kohnen and Koch 2006).

History

The iris-claw phakic IOL was initially used in aphakic eyes after intracapsular cataract extraction. Starting in 1953, the first-generation models such as the Binkhorst lens and the Medallion lens were associated with cystoid macular edema, corneal decompensation, lens dislocation, uveitis, and glaucoma. In 1978, J. Worst designed the iris-claw or "lobster-claw" IOL, a coplanar one-piece PMMA IOL, which was enclavated in a fold of mid-peripheral iris stroma, a relatively immobile portion of the iris. Many surgeons have used the iris-claw lens after intracapsular cataract extraction or as secondary implantation in aphakia. In 1986, Fechner implanted the first sighted myopic phakic eye (Fechner and Alpor 1986). Follow-up of Fechner-Worst lens implantation showed good predictability but a progressive corneal endothelial cell loss. The currently available iris-claw model is basically the original IOL with few changes.

Clinical Features

The Artisan phakic IOL is made of a single-piece, non-foldable, ultraviolet light-absorbing PMMA material. It is available for the correction of myopia, hyperopia, and astigmatism, as well as for aphakia. The optic vaults approximately 0.87 mm anterior to the iris, allowing for an important clearance from both the anterior lens capsule and the corneal endothelium. The distance from the optic edge to the endothelium ranges from 1.5 to 2 mm depending on dioptric power, anterior chamber anatomy, and diameter of the optic. There are two models available to correct myopia: model 206 has a 5.0-mm optic with power ranging from −3 to −23.5 diopters (D) in 0.5 D increments and model 204 has a larger 6.0-mm optic and is consequently limited to a smaller range of powers because of its greater proximity to the endothelium in the periphery of the IOL, −3 to −15.5 D in 0.5 D increments. For the correction of hyperopia, model 203 incorporates a 5-mm optic, and it is available in dioptric powers ranging from +1 to +12 D in 0.5 D increments. Myopic lenses require more clearance than hyperopic due to thicker peripheral edges. The thickest part of the hyperopic IOL on the other hand is central, where the anterior chamber depth is greater. Rhetoric model has a 5-mm optical zone and is available in powers ranging from +12 D to −23.5 D in 0.5-D increments, with additional cylinder from +1.0 D to +7.0 D, also in 0.5-D increments, and oriented either at 0° or at 90°. It has a fixed overall length of 8.5 mm (7.5 mm for pediatric implantations or small eyes), which is a great

advantage to the surgeon who does not wish to deal with sizing measurements.

Tests

Anterior chamber depth for Artisan/Verisyse phakic IOL implantation must be at least 2.7 mm. Other inclusion criteria for phakic IOL implantation must be considered (see also "▶ Phakic Intraocular Lens").

Differential Diagnosis

Other currently available types of phakic IOLs are anterior chamber angle (AcrySof) or posterior chamber (Phakic Refractive Lens and Implantable Collamer Lens) phakic IOLs (Hardten et al. 2003).

Etiology

On the European market, this phakic IOL is distributed as Artisan® (Ophtec B.V., Groningen, The Netherlands) and in the USA as Verisyse® (Abbott Laboratories, Abbott Park, Illinois, USA). The foldable model of the iris-claw lens is the Artiflex/Veriflex phakic IOL, which has a hydrophobic polysiloxane foldable design with a 6.0-mm optic (Güell et al. 2010).

Treatment

For Artisan/Verisyse implantation, retrobulbar or peribulbar anesthesia is recommended. A two-plane, 5.2 or 6.2-mm posterior corneal incision is centered at 12 o'clock, and two vertical paracenteses directed to the enclavation area are performed at 2 and 10 o'clock. Alternatively, scleral incision may be used. Pupil should be constricted to protect the crystalline lens from contact with the phakic lens or instruments. After the anterior chamber is filled with viscoelastic material, the lens is introduced and rotated 90° into horizontal position. The lens is fixed with an enclavation needle that has a bent shaft and a bent tip that pushes the iris into both claws. Peripheral iridectomy should be performed to prevent pupillary block situation. Alternatively, Nd:YAG laser can be used preoperatively to create one or two small iridotomies 90° apart. The corneal wound is then sutured with five interrupted 10–0 nylon stitches, the scleral incision with one running suture.

Cross-References

- ▶ Foldable Intraocular Lens
- ▶ Intraocular Lens
- ▶ Phakic Intraocular Lens
- ▶ Verisyse Iris-Supported Phakic Intraocular Lens

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Arylsulfatase B Deficiency, ASB Deficiency

- ▶ Maroteaux-Lamy Syndrome

ASA

- ▶ Aspirin (for Carotid Artery Disease)

Aspergillosis and Mucormycosis, Orbital Infections

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Definition

Aspergillosis is a group of diseases caused by a fungal infection of the genus *Aspergillus* primarily or secondarily involving the orbit.

Mucormycosis (also known as phycomycosis) is a fulminant, invasive fungal infection that can involve the orbit and that most commonly is caused by the genera *Mucor* and *Rhizopus* (Anaissie et al. 2009).

Etiology

Aspergillus is an opportunistic pathogen and invasion of the orbit most often occurs via the paranasal sinuses. Route of infection is thought to be via inhalation of *Aspergillus* conidia. Rarely, orbital infection may occur via hematogenous spread or from surgical and traumatic inoculation. Orbital infection can occur in both immunocompetent and immunocompromised hosts (Levin et al. 1996; Sivak-Callcott et al. 2004; Arndt et al. 2009). In the immunocompetent host, *Aspergillus* often causes a chronic indolent sinusitis or an allergic sinusitis characterized by chronic mucosal inflammation without frank orbital invasion (Klapper et al. 1997). In the immunocompromised host, aspergillosis may also cause a chronic indolent sinusitis, but it often leads to a rapidly progressive sinus infection with direct orbital invasion. Orbital invasion in the immunocompromised host typically occurs secondary to direct extension via paranasal sinuses although other foci of infection such as dacryocystitis have been described. Vascular invasion is rarely seen but can lead to thrombosis and tissue necrosis.

Orbital mucormycosis usually develops from direct extension of infection into the orbit from the nasal and paranasal sinus mucosa (Yohai et al. 1994; Arndt et al. 2009). These fungi have a predilection for vascular invasion, resulting in thromboses and extensive tissue necrosis. *Mucor* and *Rhizopus* are typically low virulence organisms found in soil and decaying organic material which are inhaled as conidia and colonize the nasal and paranasal sinus mucosa. Like invasive aspergillosis, mucormycosis has a strong predilection for the immunocompromised host occurring in patients with HIV, cancer, renal failure, diabetes mellitus, and in those on immunosuppressive agents (Pagano et al. 1997; Maiorano et al. 2005).

Epidemiology

Orbital aspergillosis and rhino-orbital-cerebral mucormycosis are rare, and definitive epidemiological data do not exist.

Aspergillus is an aerobic fungus that is often found as molds growing in many oxygen rich environments. In immunocompetent hosts, aspergillosis is the most common fungal sinus infection. Immunocompetent hosts rarely develop an invasive infection; however, cases have been reported. Invasive aspergillosis occurs more often in the immunocompromised host. HIV, malignancy, chemotherapy, immunosuppressive agents, diabetes mellitus, and neutropenia have been shown to be risk factors for the fulminant form of aspergillosis (Sivak-Callcott et al. 2004). Of the hundreds of species of *Aspergillus*, *Aspergillus fumigatus* is the most common species that infects the paranasal sinuses.

Similar to invasive aspergillosis, mucormycosis occurs in the immunocompromised host. An Italian multicenter review of 37 cases of patients treated for acute leukemia found that 1% had mucormycosis, although the orbit was an infrequent site of disease. Of all patients who are diagnosed with mucormycosis,

over half have poorly controlled diabetes mellitus and ketoacidosis which leads to poor neutrophil phagocytosis and increased host susceptibility to fungal invasion (Pagano et al. 1997).

Clinical Presentation

In the immunocompetent host, the presentation of *Aspergillus* infection can be varied but is rarely aggressive. Most cases present as a chronic sinusitis secondary to allergic fungal sinusitis or to chronic granulomatous inflammation resulting from a fungal ball (aspergilloma). Often patients will describe nasal discharge or facial discomfort. However, a small subset of patients with allergic fungal sinusitis may describe symptoms of orbital involvement characterized by decreased vision, diplopia, proptosis, epiphora, or cranial nerve palsies (Bray et al. 1987). Immunocompromised hosts with fulminant *Aspergillus* sinusitis may present with invasion of the face, the intracranial cavity as well as the orbit. Signs and symptoms of orbital invasion may include severe pain, decreased vision, proptosis, chemosis, and diplopia. Direct extension of infection can lead to extraocular muscle dysfunction as well as cranial nerve involvement. Orbital apex syndrome can occur and cavernous sinus thrombosis has been described.

Like invasive aspergillosis, rhino-orbital-cerebral mucormycosis may present with a variety of symptoms. Early symptoms may be nonspecific and include fever, headache, and sinus congestion or discharge and may progress to orbital and facial pain, decreased vision, diplopia, and altered mental status. Classically with mucormycosis, necrotic tissue on the nasal mucosa may appear as a black crust. In both invasive aspergillosis and mucormycosis, examination may show signs of orbital cellulitis, proptosis, chemosis, decreased ocular motility, and an afferent papillary defect (Yohai et al. 1994; Arndt et al. 2009).

Diagnostics

Diagnosis is suggested by clinical history and radiological imaging of the orbit and paranasal sinuses. Imaging also is important in monitoring for progression and in constructing a treatment plan. Samples should be obtained and sent for stains, cultures, and in vitro susceptibility testing to evaluate for amphotericin resistance. Microscopic diagnosis is the gold standard. *Aspergillus* has characteristic features including 45° branching, septate hyphae seen with Gomori methamine silvers and periodic acid Schiff stains. The fungi causing mucormycosis have irregularly branching, broad, nonseptate or sparsely septate hyphae seen with Gomori methamine silvers and periodic acid Schiff stains. Some suggest that multiple samples should be obtained both via direct tissue biopsy and via nasal debridement and sinus or abscess aspiration. Obtaining biopsy with vascular specimen may be particularly useful in histological diagnosis of mucormycosis as hyphae may be seen invading vessel walls (Anaissie et al. 2009).

Differential Diagnosis

Cavernous sinus thrombosis
Orbital pseudotumor
Sarcoidosis
Leukemic infiltration
Lymphoma
Metastatic carcinoma
Rhabdomyosarcoma
Thyroid ophthalmopathy
Wegener granulomatosis
Other vasculitides and collagen tissue disorders

Prophylaxis

Prophylactic antifungal therapy with polyenes, azoles, or triazoles has been described. Some experts suggest the use of prophylactic antifungals in patients who are expected to be severely granulocytopenic for over 7 days at institutions with high incidence of invasive fungal infections. It may also be considered for patients who will be on significant immunosuppression therapy following bone marrow or stem cell transplants.

Treatment

Prompt diagnosis and early treatment with aggressive debridement and antifungal medication is the main treatment modality. Surgical removal of necrotic tissue may require multiple surgeries and repeat imaging studies to evaluate for progression. Exenteration was the mainstay of treatment until relatively recently but is no longer considered crucial in most cases. Systemic antifungal medication should be initiated promptly and typically consists of amphotericin B at 1–1.5 mg/kg/day. After a few days of treatment it can be decreased to a maintenance dose of 0.8–1 mg/kg/day. Some experts advocate spacing treatment out to every other day once the disease is in remission. In addition to amphotericin B, the azole class of antifungals has been shown to be effective as well although efficacy data is lacking in direct comparisons to amphotericin B. Treatment may be enhanced by local injection or packing of surgical area with antifungal agents. Hyperbaric oxygen may complement surgical and antifungal therapies. Systemic antifungal treatment should continue for long after the infection is shown to be controlled. Some experts advocate indefinite treatment in immunocompromised patients. Treatment of underlying immunocompromising condition is also important when possible such as in cases of ketoacidosis.

Prognosis

Until relatively recently the prognosis was bleak with survival rates as low as 10%; however, earlier diagnosis and more aggressive management has improved survival to 65–85%. Orbital aspergillosis has a better survival rate than mucormycosis (Yohai et al. 1994). Poor prognostic indicators include delayed treatment, leukemia, hemiparesis, hemiplegia, iron chelation therapy, renal disease, and bilateral sinus involvement. Early treatment initiation is key as a review article in 1994 found that patient survival with rhino-orbital-cerebral mucormycosis was 81% when surgery was undergone within 6 days of symptoms but declined to 52% when undergone at day 7–12 and fell further to 42% when undergone between day 13 and 30. Morbidity is also high, and extensive surgical debridement often results in severe facial disfigurement.

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Aspergillosis in Orbit

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▶ Aspergillosis and Mucormycosis, Orbital Infections

Aspergillus (Aspergillosis), Endogenous Endophthalmitis

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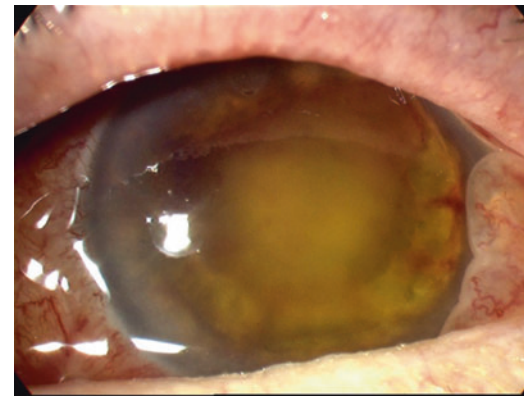
Synonyms

Endogenous endophthalmitis

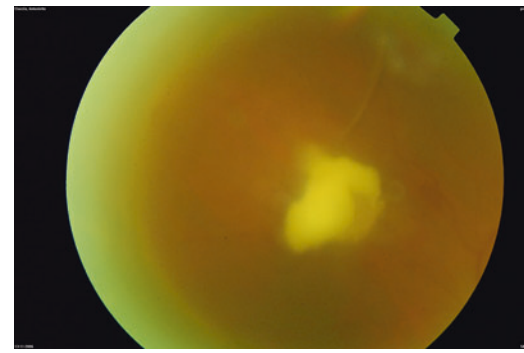
Definition

The *Aspergillus* species is a member of the deuteromycetes fungi. They are highly aerobic and are found in the air we breathe. It is commonly involved in pulmonary and paranasal sinus infections, and while it occasionally occurs in immunocompetent patients and can lead to orbital involvement and keratitis, it is most commonly related to immunocompromised patients and is the second most common cause of endogenous endophthalmitis following the *Candida* species. Risk factors for developing *Aspergillus* infection include neutropenic patients, following solid organ transplantation in those taking systemic corticosteroids or immunosuppression drugs, diabetes mellitus patients, cystic fibrosis patients, intravenous drug users, or those with an impaired immune system, such as those with human immunodeficiency virus infections. *Aspergillus flavus*, *A. fumigatus*, *A. niger*, *A. terreus*, *A. glaucus*, and *A. nidulans* have all been reported to cause endophthalmitis, with A. *fumigatus* and *A. Flavus* the most commonly identified. *Aspergillus* endogenous endophthalmitis results from hematogenous spread of the fungus from a distant, infected site, such as an infected heart valve, urinary tract, or following prolonged intravenous drug use. Alternatively, sinus involvement can result in direct spread into the orbit and later reaching the globe.

Clinically, *Aspergillus* endogenous endophthalmitis has a rapid time to presentation and is usually evident within 5 days of infection, which is much faster than other fungi such as *Candida*. Patients may complain of visual loss, red eye, photophobia, severe ocular pain, and floaters. There is a panuveitis with or without a hypopyon (Fig. 1), and there may be yellow subretinal and retinal infiltrates that preferentially affect the macula, with subhyaloid and subretinal exudation (Fig. 2). As the disease progresses, a dense vitritis may develop, obscuring the fundus. Invasion of the choroidal vessels may result in exudative or purulent retinal



***Aspergillus* (Aspergillosis), Endogenous Endophthalmitis, Fig. 1** Anterior chamber involvement



***Aspergillus* (Aspergillosis), Endogenous Endophthalmitis, Fig. 2** Macular chorioretinal lesion with overlying vitritis

detachments, with retinal involvement leading to extensive retinal necrosis that includes the optic nerve and macula in many cases. Corneal involvement and orbital involvement occur in many cases and are significant risk factors for permanent severe vision loss.

Diagnosis requires a high level of suspicion and is based on obtaining a careful history aimed at identifying patients at high risk of endogenous endophthalmitis. The definitive diagnosis and identification of the responsible pathogen are based on obtaining a vitreous sample, followed by immediate processing in order to maintain the viability of the sample. Samples should be viewed using direct microscopy following KOH preparation in order to dissolve the human cells and allow direct visualization of the fungi. The use of Gram or Giemsa staining can yield up to 90% positive identification. Cultures are needed for identification of specific fungal species and in vitro susceptibility to various antifungal agents, and samples are typically incubated for 2–4 weeks before a negative culture result is confirmed.

Vitrectomy with intravitreal injection of antifungal drugs is the mainstay for treatment of advanced *Aspergillus* endogenous endophthalmitis. It clears the vitreous of inflammatory debris and allows the obtaining of a vitreous sample for diagnosis and the administration of intravitreal drugs. While treatment approaches also involve the use of systemic antifungal agents, with amphotericin B the most widely used, these drugs have poor intraocular penetration and therefore require the addition of intravitreal injections to achieve a therapeutic dose. Other intravitreal agents, including voriconazole or miconazole, are also effective in treating *Aspergillus* endogenous endophthalmitis. Systemic voriconazole has good intraocular penetration and can be used as an alternative to amphotericin B in treating *Aspergillus*.

The outcome of these patients can be variable with immunocompromised patients faring the worst. However, the utilization of prompt diagnosis with aggressive intravitreal antifungal treatment has improved the outcome of these patients, preventing vision loss and increasing their survival.

Cross-References

- ▶ Amphotericin B, for Aspergillus Endophthalmitis
- ▶ Endogenous Endophthalmitis
- ▶ Endophthalmitis

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Aspheric Ablation Profile

- ▶ Aspheric Profile Photorefractive Keratectomy
- ▶ Q-Factor Customized Ablation Profile

Aspheric Profile Photorefractive Keratectomy

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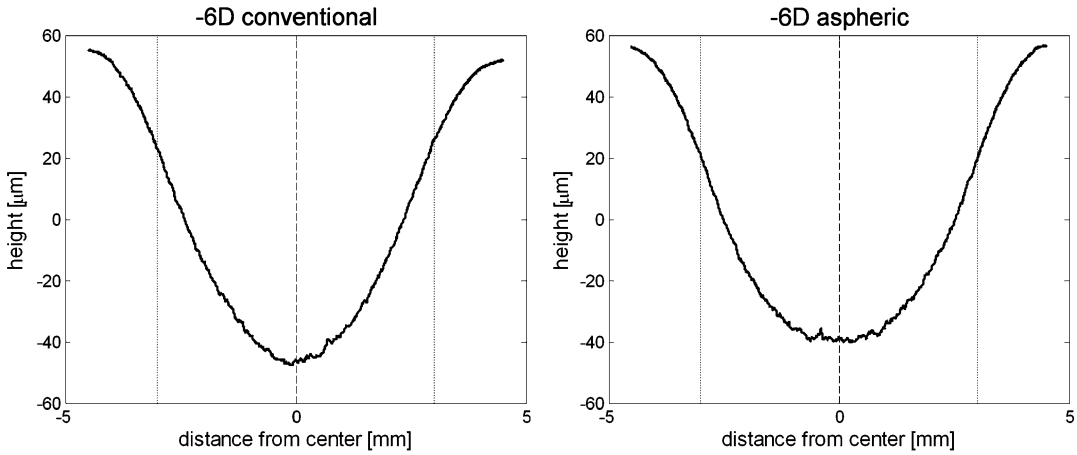
Synonyms

Aspheric ablation profile; Q factor-optimized ablation profile; Wavefront-optimized ablation profile

Definition

An ablation profile that aims at minimizing postoperative spherical aberration, either by compensating for the amount of spherical aberration expected to be induced by the ablation or by maintaining preoperative corneal asphericity (q factor) (Fig. 1).



Aspheric Profile Photorefractive Keratectomy, Fig. 1 Conventional and aspheric ablation profile for a myopic corneal ablation of -6 D

History

Corneal topographic and aberrometric measurements revealed an induction of positive spherical aberration (Applegate and Howland 1997) which was found to be proportional to the attempted spherical equivalent (Moreno-Barriuso et al. 2001; Oshika et al. 2002). This deviation of induced optical effects from Munnerlyn's formula effect was first attributed to biomechanical effects (Roberts 2000). Later, studies with PMMA lenses suggested physical rather than biomechanical effects, namely, the decrease of laser fluence in the corneal periphery (Bühren et al. 2010; Dorronsoro et al. 2006). These findings and the fact that spherical aberration significantly deteriorates retinal image quality prompted the development of aspheric ablation profiles with less induction of spherical aberration than conventional profiles (Mrochen et al. 2004). Aspheric profiles can be used both for LASIK and for surface ablation techniques. Also customized (wavefront-guided) profiles can be aspheric. Aspheric profiles for hyperopia are still under development.

Tests

Most algorithms require a preoperative corneal topography to determine the preoperative corneal asphericity (q factor). Together with other data like refraction and aberrometry, programmed optical zone, and corneal pachymetry, these data are integrated in the treatment algorithm. The treatment itself is identical to a treatment with a conventional profile. The predictability of an aspherical ablation can be checked with postoperative corneal topography or aberrometry.

Cross-References

► Corneal Ablation

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Aspherical Intraocular Lens

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Synonyms

Aberration free intraocular lenses

Definition

Aspheric intraocular lenses are defined as lenses that try to modify the spherical aberration of the optical system of the eye to achieve improved quality of vision. This is done by the modification of the curvature of at least one surface in an aspherical manner.

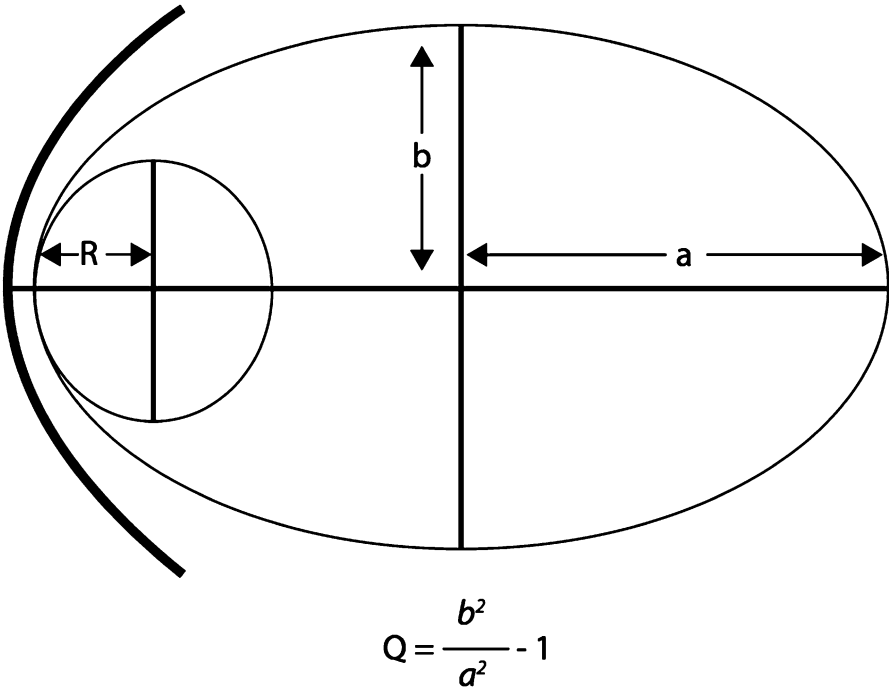
Basic Characteristics

Asphericity in IOL Optics

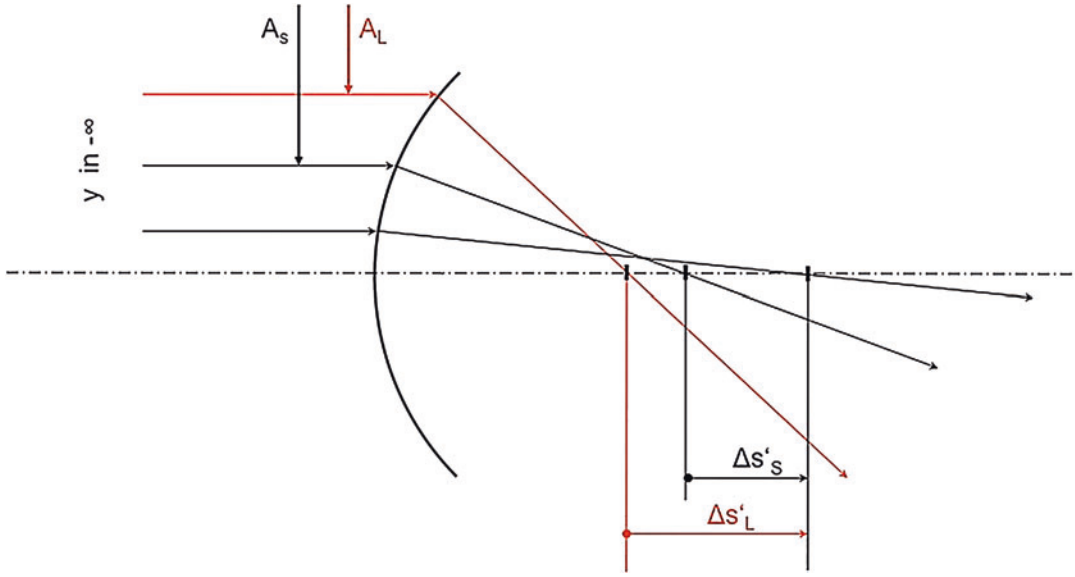
In IOLs, asphericity usually describes a lens with at least one nonspherical surface of usually rotational symmetric shape and continuously changing radii from center to periphery. An exception is any kind of toric aspheric IOL, which is not rotationally symmetric but still keeps up the same asphericity in each meridian, even with changing radii in the meridians. Asphericity is described by the Q factor, which characterizes different types of spherical, elliptic, or nonelliptic shapes. $Q = 0$ characterizes a spherical shape, $Q > 0$ an oblate ellipse, $Q < 0$ but > -1 a prolate ellipse, $Q = -1$ parabolic, and $Q < -1$ a hyperbolic shape (Fig. 1).

Spherical Aberration

Spherical aberration describes the effect of changing angles of incidence with increasing distance



Aspherical Intraocular Lens, Fig. 1 Defining the Q factor and thus asphericity of a surface by the metrics of an ellipse



Aspherical Intraocular Lens, Fig. 2 Schematic principle of spherical aberration. With increasing distance from the optical axis in lenses (not only in spherical ones) the angle of incidence changes (in this case increases) and thus refractive power increases. The result is the difference in spherical aberration (Δs') for small (*S*) and large (*L*) apertures (*A*)

from the optical axis of light rays at a lens. With increasing angle of incidence also the refractive power increases and thus the vertex power increases for peripheral rays compared to central ones (Fig. 2). This again results in an increased depth of focus but also aberrates the image. It is important to keep in mind that the effect is stronger with larger apertures (in the eye this is the pupil). For very small pupils the effect thus is, as for all aberrations, almost not existent.

Of course aspheric lenses also have a certain amount of spherical aberration. Only in the very special case of neutrality of spherical aberration, they do not suffer from it.

Mode of Action

From the cornea it is known that its asphericity and positive spherical aberration remains stable in aging. The lens however changes from negative to positive spherical aberration with age. Thus, the compensation of the cornea's positive spherical aberration decreases with age. Spherical intraocular lenses now try to modify the spherical aberration of the optical system of the eye, to increase quality of vision.

Aspheric Intraocular Lens Models

Today intraocular lenses can be divided into three major groups, when defined by their asphericity only:

1. Lenses with positive spherical aberration (all spherical lenses, but also aspheric ones)
2. Lenses with negative spherical aberration (all aspheric)
3. Lenses that do not induce spherical aberration (all aspheric)

The latter are often misleadingly marked as "aberration free lenses." However, no lens is free of aberrations, aberrations make a lens a lens. This term only refers to the spherical aberration.

Reasonable Range of Application

The effect of intraocular lens asphericity is highly dependent on pupil diameter, as spherical aberration itself is the optical aberration representing the errors induced by large apertures. Trials show that pupil sizes larger than at least 4 mm are needed to measure a decrease in spherical aberration that can provide a benefit in quality of vision. However, in what magnitude this measurable difference is of subjective

relevance for the patients is not fully evaluated yet. As cataract patients most often have very small pupils, they do hardly ever profit from aspheric lenses. As implants used in refractive lens exchange to correct ametropia of young patients with large mesopic pupils, they seem to be of more benefit.

Cross-References

- ▶ Accommodation, Cataract
- ▶ Clear Lens Exchange (CLE)
- ▶ Intraocular Lens
- ▶ Optical Quality
- ▶ Refractive Lens Exchange
- ▶ Spherical Equivalent

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Aspiration Curette

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Definition

An instrument used in cataract surgery. It was designed to polish the anterior capsule leaf efficiently and safely to reduce fibrotic after-cataract and to avoid capsular contraction syndrome.

Clinical Features

The tip of the aspiration curettes is equipped with an upward-facing, slit-like aspiration port (0.23 mm in width, 1.5 mm in length). The parallel edges of the slip are sharp; the edge at the proximal and distal turning points is rounded. The curette fits into the aspiration handpiece of a standard bimanual irrigation/aspiration set. One can differentiate between two different instrument types: one non-venting system with a sharp edge and a sharp edge venting curette.

Tests

The anterior capsule polishing with aspiration curette may be used in the eyes with pseudoexfoliation syndrome and resulting zonular weakening to reduce the capsular contraction syndrome.

Another application can be considered in the eyes with peripheral retinal disease to retain the transparency of the peripheral optic of the IOL.

Differential Diagnosis

Other methods to reduce the postoperative incidence of after-cataract:

- Sharp posterior optic edge as barrier effect, combined with a circular rhexis optic overlap
- Haptics of intraocular lense with capsular bag design and a slim junction to the optic
- Fibrosis-inducing optic materials

Treatment

See "Clinical Features" section above.

Cross-References

- ▶ After Cataract
- ▶ Anterior Capsule

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Aspirin (for Carotid Artery Disease)

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Synonyms

Acetylsalicylic acid; ASA; Bayer; Ecotrin

Definition

Acetylsalicylic acid (ASA)

Indication

Aspirin is used as an analgesic, antipyretic, anti-inflammatory, as well as an antiplatelet medication. It is used as treatment in several diagnoses that require the aforementioned medicinal properties.

Contraindication

Aspirin is generally contraindicated in patients with hypersensitivity to aspirin or any of its components, hemophilia or other active bleeding disorders, bleeding ulcers, or in a hemorrhagic state. It is relatively contraindicated in peptic ulcer disease, pregnancy, children, gout, and liver and kidney disease.

Use and Dosage

The dosage of aspirin given to treat patients depends on the indication for treatment. In treatment for coronary artery disease, it is recommended to start with low-dose aspirin. A dose of 75–100 mg per day is recommended for an indefinite period of time in these cases. This dose may be used in patients with established coronary heart disease as well as for prevention of coronary heart disease in asymptomatic patients above the age of 50. In the case of a myocardial infarction, a dose of 160–325 mg could be given immediately after the event, and a reduced dosage of 75–100 mg could be continued thereafter. In ophthalmology, although there is no proven randomized controlled clinical trial data on efficacy for neuro-ophthalmologic disease, many authors recommend aspirin in patients with vasculopathic neuro-ophthalmic disease (e.g., nonarteritic and arteritic anterior ischemic optic neuropathy, giant-cell arteritis, ischemic ocular motor cranial neuropathies, carotid and vertebral dissections, ischemic nonhemorrhagic

cerebrovascular accidents, and transient ischemic attacks including ischemic amaurosis fugax).

Adverse Reactions

Aspirin may cause several adverse effects, which include gastrointestinal bleeding, nausea, heartburn, constipation, upset stomach, dizziness, headache, and tinnitus. Studies performed evaluating the adverse effects of aspirin have found that the occurrence of adverse effects is related to dosage. With the small doses used in coronary artery disease treatment and prevention, few side effects are experienced. As the dosage of aspirin increases in patient treatment, the side effects become a more prominent barrier and obstacle for treatment.

Interactions

Aspirin has several interactions with other medications due to the fact that it acetylates albumin and therefore may alter the binding of other drugs to albumin. Aspirin may decrease the effects of ACE inhibitors, diuretics, uricosuric agents, anticonvulsants, and beta-blockers. It may increase the effects of sulfonylureas, causing hypoglycemia, as well as increase the concentration of carbonic anhydrase inhibitors and methotrexate. Aspirin may also increase the risk of bleeding when taken with other anticoagulants or nonsteroidal anti-inflammatory medications.

Cross-References

- ▶ Aspirin: Usage, Effects, and Dosage in Ophthalmology
- ▶ Atropine Drug, Usage in Ophthalmology

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Aspirin: Usage, Effects, and Dosage in Ophthalmology

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Definition

Acetylsalicylic acid.

Indication

Aspirin is used as an anticoagulant in patients with thromboembolic risk factors. Moreover, aspirin is used as an analgesic, antipyretic, and anti-inflammatory drug.

Contraindication

Allergy or intolerance to nonsteroidal anti-inflammatory drugs, gastric ulcers, liver and kidney disease, gout, hyperuricemia, glucose-6-phosphate dehydrogenase deficiency, pregnancy, and asthma.

Use and Dosage

Analgesia and antipyretic effect, 300–1,000 mg one to three times daily; anticoagulant, 75–300 mg 1/daily.

Adverse Reactions

Patients under aspirin therapy in theory have an increased risk for hemorrhagic complications when ophthalmic surgeries are performed. However, several studies have shown that vitreoretinal surgeries, cataract surgeries, glaucoma surgeries,

and intravitreal injections on systemically anticoagulated patients were not associated with significant intraoperative or postoperative bleeding complications. In patients with diabetic retinopathy, the use of aspirin does not increase the occurrence of vitreous/preretinal hemorrhages.

Interactions

Combination therapy with other anticoagulants may increase bleeding complications. Aspirin must not be applied in patients under methotrexate therapy in a dose of >15 mg/week.

Cross-References

- ▶ Cataract Surgery
- ▶ Diabetic Retinopathy
- ▶ Ghost Cell Glaucoma
- ▶ Intravitreal Injections

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Asteroid Bodies or Scintillation Nivea

▶ Asteroid Hyalosis

Asteroid Hyalitis

▶ Asteroid Hyalosis

Asteroid Hyalosis

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Synonyms

Asteroid bodies or scintillation nivea; Asteroid hyalitis

Definition

Asteroid hyalosis was first described by Benson in 1894. While minute white opacities are found in the otherwise normal vitreous, this condition presents as cream-white spherical bodies distributed throughout the vitreous either randomly or in chains or sheets. The biomolecular composition of asteroid bodies has only recently been explored, and many questions remain unanswered. The asteroid bodies feature a multilamellar structure formed of a mineral compound containing calcium, phosphorus, and oxygen, presumably a calcium apatite like material, with chondroitin-6-sulfate at the periphery and hyaluronic acid in the inner matrix.

The prevalence of asteroid hyalosis has been reported to range from 0.36% to 1.96%. In 75% of cases, the condition is unilateral, and it only rarely causes a significant decrease in visual acuity.

Clinical studies have showed associations of asteroid hyalosis with diabetes, hypercholesterolemia, hypertension, gout, increased serum calcium levels, hyperopia, male gender, and age over 50 years. Because asteroid hyalosis is basically the deposition of complexes of calcium and lipids, an association of asteroid hyalosis with serum cholesterol and serum calcium levels is credible. Yet the exact etiology of asteroid hyalosis is not known.

Although asteroid hyalosis is generally considered to have only a minor impact on visual acuity, some patients are sufficiently disturbed by their visual symptoms to undergo surgical treatment to remove opacities.

Astigmatic Keratotomy

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Synonyms

Arcuate keratotomy; Hexagonal keratotomy; Transverse keratotomy; Trapezoidal keratotomy

Definition

Corneal incision technique for reducing the grade of astigmatism by changing the cornea from a football shape to a more rounded one.

Epidemiology

Due to high levels of success with LASIK procedures, the number of astigmatic keratotomies has reduced significantly.

History

In the early nineteenth century, Shiotz, Lans, and Bates first described the astigmatic keratotomy as an incisional surgery. Troutman was one of the first surgeons who discussed the benefits of corneal incisions to decrease astigmatism. Further developments of his ideas included adding nomograms, transverse or arcuate incisions. As toric intraocular lenses and LASIK were introduced, the frequency of astigmatic keratotomy has been reduced.

Clinical Features

See "Treatment" section.

Tests

Thorough examination of the anterior segment with the slit lamp and corneal topography, pachymetry, and measurement of uncorrected and best spectacle-corrected visual acuity are mandatory to maintain best possible postoperative results. See also entries Astigmatism, PRK, LASEK, and LASIK.

Differential Diagnosis

Other types of incisional keratotomy:

- Arcuate and transverse keratotomy
- Trapezoidal keratotomy
- Hexagonal keratotomy
- Radial keratotomy
- Limbal relaxing incisions

Etiology

See "▶ History" section.

Treatment

The refractive surgeon places either a transverse or arcuate incision perpendicular to the steep axis of the cornea. The result is a flatter cornea by an increased radius of curvature in the meridian and a

steeper meridian 90° away. Incisions are between 5 and 7 mm away from the pupil center.

Cross-References

- ▶ Astigmatism
- ▶ Custom LASIK
- ▶ Limbal Relaxing Incisions

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Astigmatic Lens

- ▶ Spherocylindrical Lenses

Astigmatism

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Synonyms

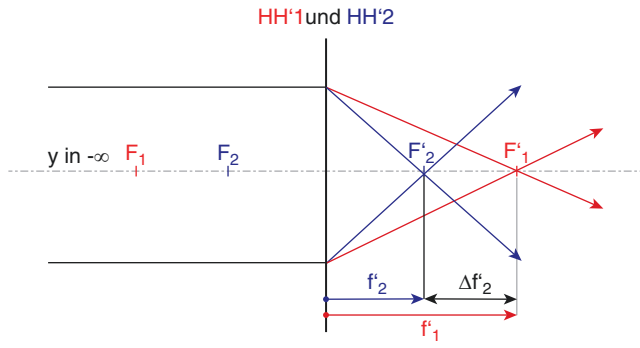
Ophthalmic astigmatism

Definition

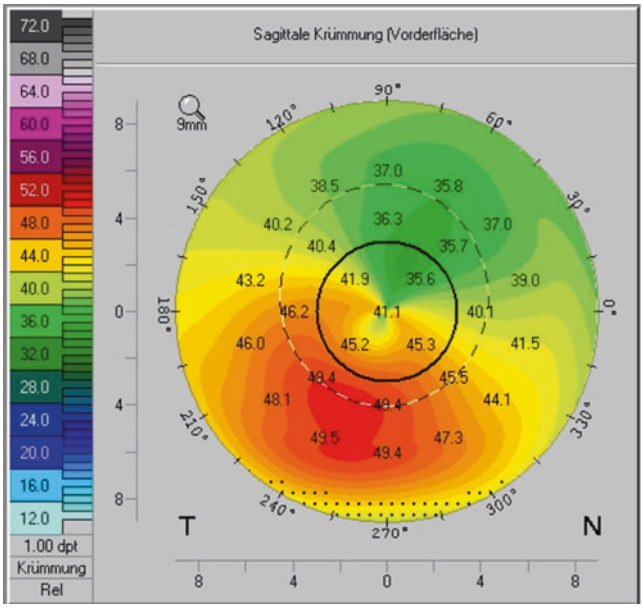
An optical system with astigmatism is one where rays that propagate in two perpendicular planes have different foci. The term comes from the Greek α- (a-) meaning "without" and στίγμα (stigma), "a mark, spot, puncture."

Basic

In ophthalmology the phrase astigmatism is used to describe the effect of toricity of the optical effective media of the eye, the cornea, and the lens. If two meridians of the respective optical system (e.g., the cornea, the anterior corneal surface, the lens, or the whole eye) with the least and highest refractive power are positioned perpendicular to each other, the resulting aberration is defined as regular astigmatism. Instead of one focal point, regular astigmatism results in two perpendicular focal lines and a circle of least confusion (Fig. 1). However, significant mild correlations were found between total and corneal astigmatism, which is why the phrase astigmatism is often used to name the entity of different curvatures in corneal meridians (McKendrick and Brennan 1996). Between the astigmatism axes of two eyes, a mirror symmetry of astigmatism (McKendrick and Brennan 1997) can often, but not always, be found.



Astigmatism, Fig. 1 Sturm's conoid, showing the principle of toric optics and resulting regular astigmatism in a positive refractive power lens, represented by the principal planes $HH'_{1,red}$ and $HH'_{2,blue}$ of its meridians 1 and 2, which are located 90° to each other. y – image. F – focal points. f – focal lengths. Δf – difference in focal lengths of the two meridians: astigmatism



Astigmatism,
Fig. 2 Topographic analysis of the corneal first surface of a keratoconic cornea, showing the typical irregular astigmatism with an inferior steepening

Characteristics

Regular Astigmatism

Regular astigmatism is defined as "with-the-rule" (WTR) when the steepest meridian of the optical system is positioned between approx. 75° and 105° and as "against-the-rule" (ATR) when the steepest meridian is positioned between approx. 165° and 195°. Astigmatism in other directions (approx. 15–75° and 105–165°) is defined as oblique.

Irregular Astigmatism

In opposite to regular appearances of astigmatism, irregular astigmatism is characterized by, e.g., three or more main meridians of the optical system (generating higher-order aberrations like trefoil, quatrefoil, etc.). This is why in clinical ophthalmology higher-order aberrations are often named irregular astigmatism. Corneal dystrophies like keratoconus also result in irregular astigmatism. This astigmatism does not follow a typical kind of regular pattern. Figure 2 shows irregular keratoconus astigmatism of the corneal first surface. A progression of corneal first surface astigmatism might be an indicator of developing keratoconus.

Correction of Astigmatism

The effect of astigmatism on visual acuity is approximately 50% of the influence of defocus and always has a negative impact on optical quality (Naeser and Hjortdal 2011). As technical optical systems can be designed easily with regular toricity, they are able to correct astigmatic aberrations of another toric optical system, just like spherical optics that correct defocus aberrations of defocused optical systems. This is the basic principle of astigmatism correction of, e.g., soft contact lenses, glasses, and toric intraocular lenses (TIOL) (Kohnen et al 2008). Other surgical options to correct astigmatism include the modification of the corneal curvature (Ortho-K contact lenses, laser in situ keratomileusis, photorefractive keratectomy, relaxing incisions, and others).

Cross-References

- ▶ Higher-Order Aberrations, Refractive Surgery
- ▶ Keratoconus
- ▶ Intraocular Lens
- ▶ ETDRS Visual Acuity Chart

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Astrocytoma

▶ Astrocytoma (Astrocytic Hamartoma)

Astrocytoma (Astrocytic Hamartoma)

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Synonyms

Astrocytoma

Definition

An astrocytic hamartoma is a benign retinal tumor occurring in the retinal nerve fiber layer that is made up of glial cells and arises from retinal astrocytes. Astrocytic hamartomas are most commonly seen in the presence of tuberous sclerosis (Bourneville disease) but may also be seen in the setting of neurofibromatosis or as solitary or sporadic lesions.

Etiology

Astrocytic hamartomas have been linked to two genetic loci TSC1 (9q34) and TSC2 (16p13) which cause the autosomal dominant disease tuberous sclerosis. TSC1 encodes for the protein hamartin while TSC2 encodes the protein tuberin. These two proteins work together to help control cell growth and size, making them tumor-suppressing genes. The mutations associated with tuberous sclerosis deactivate the tumor suppressor gene. It is thought that tuberous sclerosis, like other tumor suppressor gene syndromes, arises from the two-hit mechanism. This means that patients with tuberous sclerosis are born with a mutation in one allele of TSC1 or TSC2 and environmentally acquire a second mutation, which inactivates the second allele of that same gene.

Clinical Presentation

The majority of patients who have astrocytic hamartomas have tuberous sclerosis, characterized by a triad of seizures, mental retardation, and skin lesions. Although astrocytic hamartomas are not included in the triad, more than half of patients with tuberous sclerosis will have astrocytic hamartomas. It is estimated that around 80% of patients with astrocytic hamartomas will have them between ages 2–6 years, making it one of the first clinical signs of tuberous sclerosis. Astrocytic hamartomas most commonly occur near the optic disk; patients may present with strabismus, leukocoria, or reduced vision. A large portion of

patients with astrocytic hamartomas are asymptomatic. Astrocytic hamartomas can have different presentations depending on the location in the retina. Those seen in the periphery of the retina are usually flat, poorly defined, and semi-translucent lesions in the retinal nerve fiber layer. The lesions seen in the posterior pole are raised, opaque, white, and more nodular in appearance. These nodular lesions can become increasingly calcified and take on what is commonly referred to as a "mulberry appearance."

Diagnosis

Retinal astrocytic hamartomas can be diagnosed based on clinical appearance alone, although there are several other tests that can help support and further evaluate the diagnosis. The three main studies used for evaluating astrocytic hamartomas are optical coherence tomography (OCT), ocular ultrasonography, and fluorescein angiography (FA). Ocular ultrasonography is a noninvasive procedure that can be done to evaluate the extent of the lesion as well as any other accompanying retinal problems, such as a serous detachment. Some of the vessels in the astrocytic hamartoma are fragile and have abnormalities, making them gradually and increasingly hyperfluorescent during the FA. Lastly, the OCT will show a gradual conversion from normal retina to a hyperreflective mass with retinal disorganization and "moth-eaten" spaces. The OCT can also show the presence of additional problems, such as retinal detachments.

Differential Diagnosis

Retinoblastoma is the most important differential diagnosis to consider and rule out. Retinoblastomas will have slight differences on OCT (abrupt transition from lesion to normal retina as opposed to gradual transition seen in hamartoma) and may be differentiated on ophthalmic exam as well. Other differential diagnoses include amelanotic choroidal melanoma, retinocytoma, choroidal osteoma, juxtapapillary choroiditis, drusen, glioma, and other intraocular malignancies.

Prophylaxis

Not available.

Therapy

Anytime an astrocytic hamartoma is encountered, the patient should be sent for further evaluation of a systemic disease. Treatment for astrocytic hamartomas depends on the symptoms experienced by the patient, as most patients are asymptomatic. Therapy for astrocytic hamartomas of the retina usually involves close observation and photodocumentation, monitoring for growth and spread of the tumor. In the case that the lesion does spread or cause a retinal detachment, argon laser photocoagulation may be used to reduce the lesion as well as resolve the detachment.

Prognosis

A retinal astrocytic hamartoma is usually a benign finding but should be monitored for growth and invasion periodically. Because retinal astrocytic hamartomas are so closely tied to tuberous sclerosis, the patient should promptly be evaluated for systemic diseases. The majority of astrocytic hamartomas are asymptomatic and do not require treatment aside from close monitoring. Therefore, prognosis is usually excellent.

Epidemiology

The incidence of tuberous sclerosis is about 1/6,000–1/10,000 births. Astrocytic hamartomas are seen in approximately half of the patients with tuberous sclerosis. They also occur in neurofibromatosis or as solitary lesions, but the incidence of those cases is rare and unknown.

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Ataxia, Optic

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Synonyms

Visuomotor ataxia

Definition

Optic ataxia is a neurologic sign characterized by an impaired ability of the patient to reach and grasp visually target objects. Patients may complain of misjudging distance or difficulty localizing objects in space.

Epidemiology

The cause of optic ataxia is often unknown and prevalence difficult to estimate. It can be caused by several different diseases and is often misdiagnosed or overlooked because it frequently presents in conjunction with several other symptoms.

History

Optic ataxia was first described in 1909 by Rudolf Balint, and the Balint syndrome is characterized by three symptoms: optic ataxia, simultanagnosia, and oculomotor apraxia. For several decades it was thought that optic ataxia only occurred in the setting of Balint syndrome. It was not until 1967 that Garcin et al. first described a case of optic ataxia without simultanagnosia or oculomotor apraxia. All of Balint's patients had bilateral posterior parietal lesions, but it was later discovered that unilateral lesions could also result in optic ataxia.

Clinical Features

The main characteristic of optic ataxia is that patients have trouble reaching for and grasping visual targets in the absence of other sensory cues. The difficulties with reaching and grasping are present in the contralateral visual field. Patients who experience a left hemispheric lesion also experience difficulties reaching with the contralateral hand, regardless of the visual field. The difficulties in grasping objects are similar to those seen in cerebellar ataxia, which include overshooting and undershooting the target. Unlike patients with cerebellar ataxia, patients with optic ataxia will be able to reach the target successfully when given auditory or

proprioceptive cues to help them reach the object. The difficulty in grasping objects seems to be worse when the object is in the patient's peripheral vision as opposed to his or her point of fixation. Patients with isolated optic ataxia do not experience any visual field loss, difficulty with stereopsis, motor difficulty, or sensory difficulty.

Tests

At the moment there is no standardized exam to diagnose optic ataxia. Testing each patient's reach and grasp toward an object, such as a pencil or pen, is the exam that has been performed in most patients with optic ataxia since it was described in 1988. Another common exam performed in conjunction with reaching and grasping is drawing of objects, such as a clock, on a piece of paper. Patients with optic ataxia cannot adequately orient and localize objects, which will be reflected in their drawing. There are efforts to create a standardized bedside exam to diagnose optic ataxia. There have also been studies where patients have undergone fMRI while asked to reach, point, or grasp an object. Patients with optic ataxia will usually show lesions in the posterior parietal cortex.

Differential Diagnosis

Cerebellar ataxia, nystagmus, and visual agnosia.

Etiology

Optic ataxia is thought to be caused by a lesion in the posterior parietal cortex, more specifically in the superior parietal lobule as well as in areas around the intraparietal sulcus. Lesions in either of these two areas only cause integrative sensorimotor deficits without primary motor or sensory deficits. Optic ataxia frequently occurs within the context of Balint syndrome. Balint syndrome has several causes, including vascular infarcts, infection, and neurodegenerative and inflammatory disease. Vascular infarcts causing optic ataxia most commonly occur in the watershed regions involving the terminal branches of the middle cerebral artery and the posterior cerebral artery. The neurodegenerative diseases that can cause optic ataxia include Alzheimer disease, posterior cortical atrophy, Parkinson disease, and Creutzfeldt-Jakob disease. There have also been cases of optic ataxia caused by brain tumors that extend into the parietal region. Isolated optic ataxia is rare and is usually caused by isolated infarcts, hematomas, or localized brain injury.

Diagnosis

Patients with optic ataxia demonstrate misreaching under visual guidance to objects in their environment but can perfectly point accurately to their own body parts (e.g., touch their own nose or ear with each hand upon request).

Treatment

Treatment for optic ataxia involves treating the underlying disease. The Prognosis for recovery from optic ataxia varies depending on the etiology of the ataxia.

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Ataxia-Telangiectasia (A-T)

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Synonyms

Louis-Bar syndrome

Definition

A-T is a progressive neurocutaneous disorder that is characterized by cerebellar ataxia, dysarthria, ocular and dermatologic abnormalities, recurrent infections, and a predisposition to malignancy. A-T was first widely recognized in 1957 when two physicians wrote an eight-patient case series, and by 1963, they were able to compile a list of 101 patients.

Etiology

A-T is an autosomal recessive disease caused by a mutation in the ATM gene located in chromosome 11q22-23. Most commonly it involves a nonsense mutation, which leads to an early termination of translation and a highly unstable and rapidly degradable protein. Most mutations that cause A-T are unique, so patients who have the disease have inherited one mutation from each parent, making them a compound heterozygote. The ATM protein is a serine/threonine kinase and phosphorylates approximately two-dozen substrates, including p53. Most of the substrates' functions are DNA repair, transcription regulation, and response to oxidative stress. Due to the deficiency of the ATM protein, these substrates do not get phosphorylated and cannot function at an optimal level.

Clinical Presentation

The first sign of A-T is usually seen when the patient presents with ataxia when learning to walk. Patients will usually begin to walk at a normal age, but then experience instability with walking that becomes slowly progressive. This symptom usually leads to a misdiagnosis of cerebral palsy, episodic ataxia, or other encephalopathies. It will be observed that children prefer to run and will do so on a more narrow base, because it provides them the most stability while walking. By 8–12 years of age, most children are confined to a wheelchair. The other signs and symptoms of the disease can develop at different moments in the patient's life, but most are apparent by the age of ten. Patients will also begin to experience choreiform movements, dysarthria, difficulty swallowing, recurrent infections, lymphoid malignancies, and ocular abnormalities. Patients are found to have a deficiency in IgG2, IgE, and IgA and experience recurrent sinopulmonary infections. They have a substantial increased risk of lymphoreticular malignancy as well as sensitivity to radiation therapy. The ocular

abnormalities seen in A-T include ocular telangiectasia, strabismus, abnormalities in saccade and pursuit, nystagmus, poor convergence ability, and optokinetic nystagmus abnormalities. Ocular telangiectasias first appear in the exposed areas of the medial and lateral bulbar conjunctiva. Mental status is normal in most cases.

Diagnosis

Most patients are diagnosed around the age of ten when all of the symptoms are apparent. The symptom that most commonly leads to ocular diagnosis is the presence of ocular telangiectasia. Ocular telangiectasia presents about 4–5 years, on average, after the presentation of the first symptom, most commonly ataxia. Three routine tests are easily available to help support a diagnosis of A-T: serum alpha fetoprotein (AFP), karyotyping, and immune status of B and T cell compartments. The majority of patients (>95%) will have an elevated AFP. T cells are unusually low, although some patients may show only minor deficiencies. Gamma and delta T cells are unusually elevated in these patients, and B cells are normal to slightly elevated. Patients will also show deficiencies in IgE, IgA, and IgG2. Cerebellar atrophy will also be present on MRI, due to the depletion of Purkinje cells. A molecular diagnosis has been conceived, but due to the large size of the gene and the occurrence of unique mutations, it is very labor intensive and not routinely performed.

Differential Diagnosis

Cerebral palsy, acute infectious or episodic ataxia, malignancy, and mitochondrial disorder.

Therapy

Unfortunately there is no cure for A-T and therapy remains supportive. The goal of treatment in this disease is to manage signs and symptoms such as infections and the physical limitations experienced by the patient. Neurorehabilitation may be useful for patients and can involve speech, physical, and occupational therapy. Certain medications, such as fluoxetine and amantadine, can be used to help patients with their incoordination and imbalance. Patients will also receive medications such as propranolol to help with their tremor. When using medications in these patients, side effects must be monitored closely, and medications must be constantly reevaluated due to the appearance of new diseases and therapies, such as malignancy.

Prognosis

Life expectancy in patients with A-T is highly variable; some patients may live into the sixth decade. The three main causes of death in patients with A-T are malignancy, infection, and pulmonary failure.

Epidemiology

A-T has an incidence in the United States as high as 1/30,000–1/40,000 live births. The incidence usually ranges from 1/30–40,000 live births to 1/300,000 live births.

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Atopic Dermatitis

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Definition

A chronic, relapsing inflammatory skin disorder caused by hypersensitivity to common allergens; usually seen in individuals with a personal or family history of other atopic disorders such as asthma and allergic rhinitis.

Etiology

The precise etiology is unknown, but is likely related to IgE sensitization and disruption of epithelial barrier function. It is commonly seen in conjunction with other allergic conditions, including food allergy, asthma, and allergic rhinitis. Flares are often associated with stress, seasonal changes, and staphylococcal colonization. Patients with eyelid dermatitis frequently have associated disorders, including allergic contact dermatitis.

Clinical Presentation

Patients traditionally present with eczematous eyelid lesions associated with intense pruritus, xerosis, and lichenification. Lesions tend to be bilateral and symmetric. Other commonly affected areas include the cheeks, perioral region, antecubital fossae, and popliteal flexures. Patients with atopic dermatitis are also susceptible to ocular surface disorders, including atopic keratoconjunctivitis, neovascularization, cicatrization, and herpetic keratitis. Aqueous tear deficiency and meibomian gland dysfunction are frequently observed.

Diagnosis

Atopic dermatitis is usually diagnosed based on clinical criteria. These include typical relapsing and remitting course, early age of onset, typical age-related shifts in lesion distribution, pruritus, xerosis, and personal or family history of atopic disease. An adult onset variant does exist but is extremely rare. Atopic dermatitis is a diagnosis of exclusion, and entities listed in the differential section should be ruled out. Total IgE is often elevated but is neither sensitive nor specific. Patch testing may be pursued to evaluate for allergic contact dermatitis. KOH scrapings are occasionally performed to rule out *tinea*. Biopsy findings are nonspecific.

Differential Diagnosis

Allergic contact dermatitis
Irritant contact dermatitis
Seborrheic dermatitis
Blepharochalasis
Dermatomyositis (Heliotrope rash)
Periocular rosacea
Psoriasis
Tinea
Lichen simplex
Mycosis fungoides
Scabies
Phototoxicity/photoallergy

Prophylaxis

Early use of probiotics may protect against sensitization, but evidence is not conclusive.

Therapy

Therapy includes medications, trigger avoidance, and other behavioral modifications. Skin moisturizers and topical steroids are first-line treatments. Immunomodulators such as tacrolimus are considered second line. Short courses of antibiotics may be useful when over-colonization by *Staphylococcus aureus* is suspected. Non-sedating antihistamines may provide pruritus relief. Use of humidifiers and mild laundry detergents may also help. Many ophthalmic drops, particularly those with benzalkonium chloride preservatives,

are potential triggers. It is important to remember that allergy to both topical corticosteroids and tacrolimus is possible.

Prognosis

Symptom relief can be achieved, but exacerbations are common. Corneal neovascularization and epithelial defects associated with atopic keratoconjunctivitis must be managed aggressively to prevent serious ocular sequelae.

Epidemiology

Atopic dermatitis is common, affecting 10–15% of children and 2–10% of adults. Eyelid finding is seen in a modest portion of these patients, and the risk of lid involvement increases with age. Eighty-five percent of cases manifest within the first year of life and 95% manifest before the age of 5.

Cross-References

- ▶ Contact Dermatoblepharitis
- ▶ Dermatitis
- ▶ Keratoconjunctivitis: Overview
- ▶ Pannus/Micropannus
- ▶ Staphylococcus

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Atrophic Retinal Holes

- ▶ Retinal Hole

Atrophic Retinal Tears

- ▶ Retinal Hole

Atrophy, Geographic

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Synonyms

GA; Geographic atrophy

Definition

Well-defined area of retinal pigment epithelium (RPE), outer retinal layer, and choriocapillaris atrophy developing secondary to non-exudative age-related macular degeneration (AMD).

Etiology

Retinal pighment epithelium (RPE) atrophy represents a downstream pathogenetic pathway in various retinal diseases (see "Differential Diagnosis"). In the elderly, it is most frequently associated with non-exudative AMD and it then terment geographic atrophy (GA). While various pathways may be involved, the precise pathogenesis in the context of AMD is yet unclear.

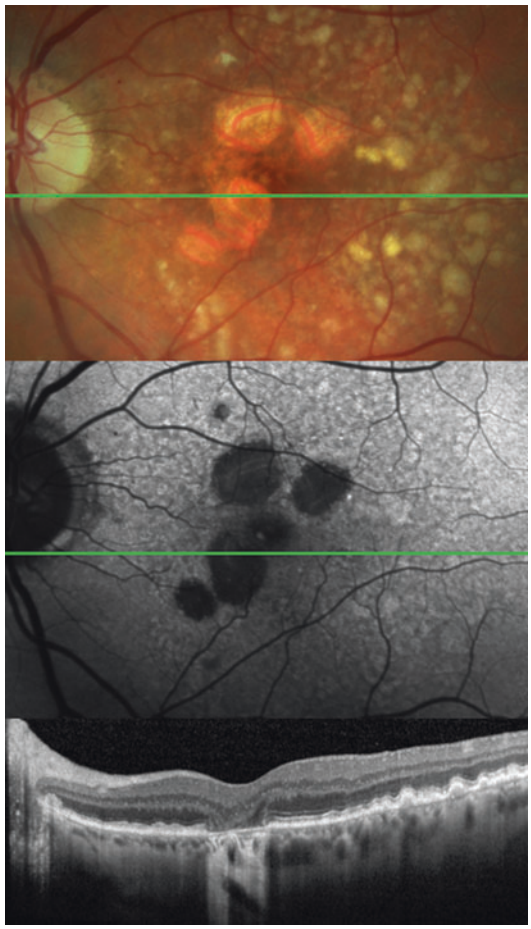
Clinical Presentation

Fundoscopically, GA appears as a sharply demarcated area with depigmentation and enhanced visualization of larger deep choroidal vessels. GA may occur unifocal or multifocal. The horizontal configuration may vary including roundish or oval to lobular patterns. Over time, GA enlarges in size, frequently sparing the fovea

unitl late in the disease process for yet unknown reasons ("foveal sparing phenomenon"). Areas of GA are associated with a corresponding absolute scotoma. Therefore, development and progression of GA is associated with vision loss (Holz et al. 2013, Fig. 1).

Diagnosis

Due to RPE atrophy and, thus, loss of intrinsic fluorophores at the level of the retinal pigment epithelium, GA is associated with a marked decrease in fundus autofluorescence (FAF) signal. This allows for more precise delineation of the atrophic areas as compared to fundus photography (Schmitz-Valckenberg et al. 2009). On SD-OCT imaging, GA is characterized by loss of the outer retinal layers, including the outer nuclear layer, the external limiting membrane, ellipsoid zone, myoid zone, and interdigitation zone, respectively, and by loss of the inner part of the RPE/Bruch's membrane complex (assumed RPE-layer; Holz et al. 2013, Fig. 1).



Atrophy, Geographic, Fig. 1 Fundus photography, fundus autofluorescence, and spectral domain optical coherence tomography (*top* to *bottom*) of a patient with geographic atrophy due to AMD showing the characteristic findings. Besides the atrophic area, also drusen and pigmentary changes are visualized. *Green line* indicates the position of the OCT-Scan

Differential Diagnosis

While only RPE atrophy secondary to non--exudative AMD is termed GA, it may be associated with a multitude of other retinal diseases, including Stargardt macular dystrophy, central areolar chorioretinal dystrophy, maternally inherited diabetes and deafness syndrome, pseudoxanthoma elasticum, late-onset retinal dystrophy, and several others. Careful recording of the history including onset of symptoms, non-ocular complaints, and family history can help to identify the underlying disease (Saksens et al. 2013). Furthermore in FAF, the area surrounding the GA may show different patterns of abnormal autofluorescence which allows for subclassification as well as differential diagnosis of GA (Schmitz-Valckenberg et al. 2009). In contrast to "pure" or "primary" GA, RPE atrophy may develop secondary to, e.g., neovascular AMD, central serous retinopathy following laser treatment, photodynamic therapy, or intense anti-VEGF therapy.

Prophylaxis

See underlying disease causing RPE atrophy.

While the AREDS trial showed a reduction in progression from intermediate AMD to neovascular late-stage manifestations by supplementation with β-carotene, vitamins C and E, and zinc, no beneficial effect on development or progression of GA was observed (Aronow and Chew 2014).

Therapy

There is no established therapy yet. Current approaches include visual cycle inhibitors, neuroprotective agents, complement inhibitors, and anti-inflammatory drugs (for review, see Holz et al. 2014).

Prognosis

GA secondary to AMD shows a progression of 1.3–2.6 mm^2 per year on average (Holz et al. 2013). The atrophic process is typically continuous and is not limited to the macular area. Central vision may be preserved for some time due to foveal sparing. However, despite good central vision, marked visual impairment may be present due to parafoveal scotoma, which, for example, strongly impairs reading and recognition of faces.

Epidemiology

The advanced form of dry AMD, or GA, is responsible for approximately 20% of all legal cases of blindness in North America with increasing incidence and prevalence due to a higher life expectancy.

Cross-References

- ▶ Optical Coherence Tomography
- ▶ Retina, Structure of

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Atrophy, Gyrate

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Synonyms

Gyrate atrophy of the choroid and retina

Definition

A rare genetic choroidal disease characterized by thinning and atrophic appearance of the choroid, retinal pigment epithelium (RPE), and outer retina in the mid-periphery and periphery of the fundus that may lead eventually to total atrophy of the choroid.

Etiology

Gyrate atrophy is an inherited disorder transferred as an autosomal recessive trait, although dominant cases have also been reported (Ryan et al. 2013). Patients have a deficiency of the enzyme ornithine-delta-aminotransferase (OAT), a mitochondrial-encoded enzyme with B_6 as a cofactor that catalyzes the interconversion of ornithine, glutamate, and proline. This results in an increase in the concentration of plasma ornithine to 10–15 times the normal levels and reduction in plasma lysine, glutamine, glutamate, and creatine. A number of different mutations have been identified within the OAT gene on chromosome 10.

Clinical Presentation

Symptoms usually begin in the second and third decades. They include poor night vision and

constricted peripheral vision. Most patients have posterior subcapsular cataracts by the end of the second decade. Myopia is also frequently observed and vitreous opacities may be present. Visual acuity loss is a later complaint in the disease, as structural changes spread from peripheral to central locations (OMIM 2010; Retina and Vitreous 2015–2016).

Fundus changes in gyrate atrophy begin in the mid-peripheral and peripheral retina with thinning and atrophy of the RPE, with the underlying choroidal vessels appearing normal or sclerotic. These areas are characteristically scalloped in shape and separate but tend to become confluent with progression of the disease. The fundus appears hyperpigmented. Additional changes with progression of the disease include pigment clumping, RPE and choriocapillary atrophy, and eventually total atrophy of the choroid, exposing the white sclera. In late stages, an annular ring of choroidal atrophy may be seen from the periphery to the posterior pole of the retina, usually sparing its center – the macula. In later stages, retinal vessels may appear attenuated and the optic disc may appear pale. There are reports of cystoid macular edema (CME) in patients with the disease. Visual function varies and depends on the extent of fundus involvement.

It was shown that type II muscle fibers were atrophic in patients with gyrate atrophy and had tubular aggregates. However, no muscle symptoms are reported, although some patients showed impaired performance when speed or acute strength was required. With disease progression, there is almost complete loss of type II fibers, which is slower than the progression of the ocular pathology.

Other reported features included mental retardation, as well as MRI changes characteristic of degenerative lesions in the white matter and premature atrophic changes.

Diagnosis

The clinical diagnosis can be confirmed by measuring serum or plasma ornithine levels. Molecular confirmation can be obtained by mutational analysis of the OAT gene.

Visual field testing most commonly shows a concentric peripheral constriction of the visual field. With time, an annular ring and paracentral scotomas may develop. With foveal involvement, a central scotoma may be seen.

Full-field electroretinogram (ERG) testing shows a mild abnormality in the amplitude of rods and cones (photoreceptor cells of the retina). With disease progression, the ERG responses deteriorate and may eventually become undetectable. Dark adaptation testing is also abnormal, with mild threshold elevations in the beginning and eventually significant elevation in most patients. The electrooculogram (EOG) is normal or only mildly reduced at the early stages of the disease, but in later stages, it is markedly reduced. Muscle biopsy shows atrophic type 2 muscle fibers with tubular aggregates visible on electron microscopy. Histopathology shows early changes in RPE cells, with subsequent loss of photoreceptors and choriocapillaries.

Differential Diagnosis

It is important to distinguish gyrate atrophy from retinitis pigmentosa (RP). RP is a group of inherited disorders in which abnormalities of the photoreceptors lead to progressive visual loss. Symptoms resemble those of gyrate atrophy and include night blindness and loss of peripheral vision and eventually of central vision. The main distinguishing features between the diseases are the hyperornithemia of gyrate atrophy, as well as the fundus appearance. In RP, there is RPE hyperpigmentation in the form of "bone spicules," attenuation of arterioles, and waxy pallor of the optic disk.

Another important entity to be distinguished from gyrate atrophy is choroideremia, a hereditary chorioretinal dystrophy. Patients present with night blindness and constricted visual fields. There is diffuse and progressive degeneration of the RPE and choriocapillaries. It first manifests as mottled areas of pigmentation in the anterior equatorial region of the retina and the macula. The anterior areas gradually degenerate to confluent

scalloped areas of RPE and choriocapillary loss, with preservation of larger choroidal vessels. The finding of generalized hyperpigmentation of the remaining RPE in gyrate atrophy, as well as the hyperornithemia, helps to distinguish it clinically from choroideremia.

Prophylaxis

Since the disease is genetically inherited, no prophylaxis can prevent its occurrence. However, an arginine-restricted diet may slow its progression (see section "Therapy").

Therapy

Since ornithine is produced from other amino acids, primarily arginine, an arginine-restricted diet appears to have therapeutic value. Studies have shown that such diet started at an early age might appreciably slow the progression of the chorioretinal lesions and, to a lesser extent, the progressive loss of retinal function.

Orally administered vitamin B_6 can result in a reduction in plasma ornithine levels in some patients, while others are nonresponsive to such treatment. Those that respond to B_6 treatment show better maintained ERG responses.

For patients with CME, a short-term therapeutic effect was shown with the use of intravitreal triamcinolone acetonide injection. After drug clearance, the edema recurred, with return of decline in visual acuity to pretreatment level.

Prognosis

The prognosis in gyrate atrophy is poor, as with time the disease advances, with progressive loss of visual field and visual acuity. The arginine-restricted diet may slow disease progression, although it is very difficult to maintain.

Epidemiology

The prevalence of gyrate atrophy was reported to be 1:50,000 in Finland, where the incidence of the disease is highest. The estimated frequency of heterozygotes is 1:110 individuals. More than 200 confirmed cases have been published in the literature so far.

Cross-References

- ▶ Atypical Retinitis Pigmentosa (RP)
- ▶ Cataract Surgery
- ▶ Carbonic Anhydrase Inhibitors, for Cystoid Macular Edema
- ▶ Electrooculogram
- ▶ Electroretinogram
- ▶ Pathologic Myopia

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Atropine Drug, Usage in Ophthalmology

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Definition

Anticholinergic/antimuscarinic drug.

Indication

Dilation of the pupil and cycloplegia for diagnostic (eye examination, cycloplegic refraction) or

therapeutic (uveitis, inflammation after surgery) reasons. Atropine penalization may also be applied in the treatment of amblyopia.

Contraindication

Known sensitivity or allergy to any ingredient of atropine eye drops.

Use and Dosage

Atropine 1% eye drops are usually applied one to four times a day.

Adverse Reactions

Blurred vision, sensitivity to light, lacrimation, hyperemia, edema or inflammation of the conjunctiva, stinging and burning, dizziness, fainting, change in heart rate, flushing of the skin, dryness of the mouth, giddiness, mental confusion, lightheadedness, vomiting and nightmares, and difficulty urinating. In patients with narrow iridocorneal angles, atropine eye drops may cause acute angle closure.

Interactions

The effect of antimuscarinic medicines may be enhanced by the concurrent administration of other medicines with antimuscarinic properties (e.g., amantadine, antihistamines, butyrophenones, phenothiazines, tricyclic antidepressants).

Cross-References

- ▶ Acute Angle Closure
- ▶ Cyclopia
- ▶ Nutritional Amblyopia
- ▶ Uveitis in Multiple Sclerosis

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Atypic *Mycobacteria* Keratitis

▶ Mycobacterium chelonae Keratitis

Atypical Bobbing

▶ Ocular Bobbing

Atypical Granular Corneal Dystrophy

▶ Reis-Bücklers Dystrophy

Atypical Retinitis Pigmentosa (RP)

▶ Retinitis Punctata Albescens

Autoimmune Retinopathies

▶ Cancer-Associated Retinopathy

Autosomal Dominant Drusen

▶ Doyne's Honeycomb Dystrophy

Autosomal Dominant Optic Atrophy

▶ Toxic/Nutritional and Hereditary Optic Neuropathy

Autosomal Recessive Optic Atrophy

▶ Toxic/Nutritional and Hereditary Optic Neuropathy

Avellino Dystrophy

▶ Corneal Dystrophies

AVM

▶ Arteriovenous Malformations (AVMs)

Avulsion

▶ Eyelid Trauma
▶ Penetrating Eyelid Injuries

Axenfeld-Krukenberg Spindle

▶ Krukenberg Spindles

Axenfeld-Rieger Syndrome; Mesodermal Dysgenesis; Leukomas

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Synonyms

Anterior chamber cleavage syndrome; Mesodermal dysgenesis of the cornea and iris

Definition

Axenfeld-Rieger syndrome (AR) is a spectrum of anomalies involving the peripheral anterior segment, iris, and systemic features, previously designated as three separate entities: Axenfeld's anomaly, Rieger's anomaly, and Rieger syndrome.

Etiology

AR is typically associated with autosomal dominant inheritance, and frequently a family history of AR is reported; however, sporadic cases are common.

Clinical Presentation

AR is usually bilateral, without sex or race predilection and diagnosed from birth to adulthood. A typical but not pathognomonic finding is posterior embryotoxon. Other exam findings include high peripheral iris strands (which are adherent to the posterior embryotoxon), ectropion uveae, iris stromal thinning, abnormally shaped pupils or decentered pupils (corectopia), and/or the appearance of multiple pupils (polycoria).

Systemic defects include dental anomalies (microdontia, hypodontia, and anodontia), craniofacial anomalies (maxillary hypoplasia with midface flattening), skeletal anomalies (short stature), umbilical anomalies cardiac anomalies, deafness, and mental retardation.

Diagnostics (Lab Diagnostics)

Diagnosis of AR is based primarily on clinical exam. Genetic studies could be considered as some genes have been identified (PITX2, FOXC1, REIG2).

Differential Diagnosis: Iridocorneal endothelial syndrome, Peter's anomaly, Aniridia, Posterior polymorphous dystrophy, Iridogoniodysgenesis, Oculodentodigital dysplasia, Ectopia lentis et pupillae, Ectropion uveae, Uveitic glaucoma, Iris coloboma, Iridodialysis, Iridoschisis

Therapy: Detection and management of glaucoma is imperative. Typically medical therapy is maximized first and surgical intervention considered later (trabeculectomy and glaucoma drainage device implantation).

Prognosis

Occasionally the central iris changes will progress in AR; however, the peripheral iris and angle changes typically do not. About 50% develop glaucoma which typically begins in childhood or young adulthood and can be challenging to control. The development of glaucoma is secondary to trabeculodysgenesis (not peripheral anterior synechiae or angle changes).

Epidemiology

AR is inherited in an autosomal dominant fashion.

Cross-References

► Posterior Embryotoxon, Neurocristopathy

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Axial Chromatic Aberration

► Chromatic Aberration: Definition

Axial Length

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Definition

Distance from the anterior curvature of the cornea to the retinal pigment epithelium in alignment along the optical axis of the eye.

Basic Characteristics

Final axial length is normally reached during the emmetropization process of the eye. Shorter axial length is associated with a hyperopic refractive error of the eye; longer axial length is associated with a myopic refractive error of the eye. Measurement of axial length is one of the most crucial steps in intraocular lens power calculation since an accuracy of <0.1 mm would result in a significant refractive error. Axial length can either be assed by ultrasonic contact biometry or by optical biometry applying partial optical coherence interferometry. Axial length assessed in ultrasonic biometry is usually shorter than axial length measured with optical biometry, since ultrasound measures the distance from the corneal surface to the internal limiting membrane of the retina, while optical biometry measures the distance from the anterior surface of the cornea to the retinal pigment epithelium.

Cross-References

► Cataract Surgery
► Emmetropia: Definition
► Optical Biometry
► Partial Coherence Interferometry

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B

Bacteria, Endophthalmitis Caused by, Endogenous

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Synonyms

Endogenous infectious endophthalmitis; Metastatic endophthalmitis

Definition

An infection of the intraocular cavities, i.e., the vitreous and/or aqueous humor, resulting from a hematogenous spread of bacteria, fungi, or protozoa.

Etiology

Endogenous endophthalmitis is the result of a hematogenous spread of an infection from a distant location in the body (most commonly endocarditis or urinary tract infection) or the insertion of a pathogen via medical devices such as needles and urethral or intravenous catheters.

Endogenous endophthalmitis is more common in the presence of chronic immune-compromising illnesses or following immunosuppressive treatment.

Pathogens

Bacterial Endogenous Endophthalmitis

Usually causes a more acute and rapidly progressive fulminant infection.

Unlike exogenous endophthalmitis, the most common pathogens in endogenous endophthalmitis are gram-positive bacteria such as:

- *Streptococcus pneumoniae* – commonly secondary to meningitis.
- *S. viridans* – commonly secondary to endocarditis.
- Other *Streptococcus* spp. such as:
  - Group G *Streptococcus*, appearing in older patients with skin wounds or malignancies
  - Group B *Streptococcus*, noted to be found in neonates with meningitis
- *S. aureus* – commonly secondary to cutaneous infections.
- *B. cereus* such as *Salmonella* and *Campylobacter* – most commonly found in IV drug abusers. These cases may present with a typical ring-shaped corneal ulcer and a brownish anterior chamber exudate.

U. Schmidt-Erfurth, T. Kohnen (eds.), *Encyclopedia of Ophthalmology*,
https://doi.org/10.1007/978-3-540-69000-9

Less commonly found are the enteric gram-negative pathogens:

- *Klebsiella pneumoniae* – most common of the gram-negative pathogen
- *Escherichia coli*
- *H. influenza*
- *P. aeruginosa*
- *Serratia* spp.

Slowly progressive or late-onset disease may be caused by:

- *Listeria monocytogenes* – infection is characterized by a brownish hypopyon and should be considered in the absence of corneal involvement (as opposed to *B. cereus*).
- *P. acnes*, though commonly related to postsurgical endophthalmitis, was described in several case reports depicting endogenous spread.

Fungal Endogenous Endophthalmitis

Fungal infections account for 50–60% of cases of endogenous endophthalmitis and are more common in immunosuppressed patients. Such infections may be more indolent than bacterial endophthalmitis, with signs and symptoms that progress over weeks:

- *Candida albicans* by far is the most common pathogen of this group, accounting for 70–80% of fungal endophthalmitis.
- *Aspergillus* is the second most common pathogen and may be present in immunocompromised patients after an organ transplant, leukemia patients, and IV drug users.
- Infection by other *Candida* species has been reported.

Viral endophthalmitis is virtually nonexistent as it usually causes uveitis.

Clinical Presentation

Endogenous endophthalmitis can occur as early as a week or as late as a month after the onset of a systemic infection.

It can present as an anterior (focal or diffuse) or posterior (focal or diffuse) panophthalmitis. It begins most commonly as a focal or multifocal chorioretinal lesion that spreads into the vitreous.

The severity and onset of symptoms may vary depending on the size of the inoculum and the type and virulence of the infective pathogen. Presentation may vary from a minimal inflammation with conjunctival injection and mild anterior uveitis to mild vitritis presenting with "snowball" opacities (especially with fungi) and even severe panophthalmitis with hypopyon, fulminant vitritis, and retinal or choroidal lesions. Rapidly progressive endophthalmitis can lead to blindness and phthisis bulbi. Furthermore, fulminant uncontrolled endophthalmitis can eventually cause cavernous sinus thrombosis, which may result in patient mortality.

Symptoms

Systemic symptoms: consistent with sepsis such as weakness chills and general malaise.

Ocular Symptoms

- Visual loss or impairment
- Pain and/or irritation
- Photophobia
- Ptosis

Suspicion of endogenous endophthalmitis should be raised in any immunosuppressed or postsurgical patient with these symptoms.

Signs

Systemic signs: consistent with sepsis, ranging from mild fever to septic shock.

Ocular Signs

- Eyelid edema and erythema
- Purulent discharge
- Conjunctival and scleral injection
- Chemosis
- Corneal edema
- Microabscesses
- Keratic precipitate (KP)
- Anterior uveitis – presenting as cells and/or flair
- Hypopyon
- Iris nodules

- Reduced or absent red reflex
- Vitritis – presenting as cells, haze, snowballs, and/or snowbanks (in cases of fungal hyphae)
- Papillitis
- Chorioretinal lesion – initially flat or only slightly elevated
- Cotton-wool spots
- Roth spots
- Retinal vasculitis
- Proptosis (in late and chronic endophthalmitis)

Epidemiology

The incidence of all types of endophthalmitis is 5/10,000 hospitalizations, with endogenous endophthalmitis accounting for 2–15% of cases. Endogenous endophthalmitis is becoming more common, as treatment with immunosuppressive and chemotherapeutic agents is constantly rising, and the numbers of AIDS patients are on the rise.

Twenty-five percent of endogenous endophthalmitis cases are bilateral. In unilateral cases, the left eye is twice as commonly affected than the right one. This is probably due to the relative proximity of the left common carotid artery to the left ventricle.

Risk Factors

Underlying Medical Condition
- Diabetes mellitus
- Malignancy and lymphoproliferative disorders
- Chronic obstructive pulmonary disease
- End-stage renal disease
- Human immunodeficiency virus (HIV) infection
- Endocarditis
- Hepatobiliary tract infections
- Skin infections
- Joint infections
- Gastrointestinal tract infections

Iatrogenic Factors
- Immunosuppressive drugs
- Intravenous and intraurethral catheters
- Recent extended surgical procedures
- Parenteral alimentation

Patient Characteristics
- Intravenous drug abuse
- Alcoholism
- Gender – in some studies a slightly higher incidence that was found in male subjects

Diagnosis

Diagnostic tests comprise ocular and systemic examination. While the former are centered on validating the diagnosis and following the progression of the disease, the systemic tests are aimed at locating the origin of the infection.

Systemic Diagnosis

General physical examination – for signs of systemic illnesses and injuries

Lab Work
- Complete blood count – for signs of infection, immunosuppressive or septic state
- Creatinine and BUN
- Erythrocyte sedation rate and CRP – to assess signs of chronic inflammation and malignancy
- Blood cultures
- Urine cultures
- Intravenous or intraurethral catheter cultures
- Other suspected infection site cultures (pharyngeal, cerebrospinal fluid, sputum, etc.)

Imaging

In the absence of a known infection site, the following imaging tests are recommended:

- Chest X-ray
- Transesophageal echocardiogram – to rule out heart valve vegetations and malformations
- Abdominal and/or chest computed tomography (CT) – to rule out perinephric or prostatic abscess

Ocular Diagnosis

- Full ocular exam and fundoscopy
- Ocular ultrasound – in cases of significant media opacities, in order to assess vitreal and choroidal involvement
- Orbital CT/MRI

- Vitreous and/or aqueous tap – for smears and culture
- Polymerase chain reaction (PCR) – for rapid diagnosis of specific pathogens

Differential Diagnosis

- Chorioretinal infection (such as CMV retinitis, toxoplasmosis, and *Pneumocystis jirovecii* (*P. carinii*), etc.)
- Noninfectious posterior or intermediate uveitis
- Neoplastic conditions
- Vitreous hemorrhage

Therapy

Although the prognosis of endogenous endophthalmitis patients is often less than encouraging, quick diagnosis and aggressive treatment may be the key to prevent severe visual loss.

Ocular Treatment

As swift and aggressive treatment is needed, when a substantial suspicion of endogenous endophthalmitis arises, often the first procedure performed is **tap** and **inject**, a bedside procedure where the "tap" refers to obtaining 0.1 cc of vitreous for culture and smears and the "inject" refers to the injection of an initial empiric antimicrobial therapy (usually vancomycin and ceftazidime). In cases in which it is unclear whether the pathogen is bacterial or fungal, empiric treatment of both etiologies is required. Additional treatment is later adjusted and added according to the culture, smear, or PCR results.

Commonly, the empiric antibiotic regimen of choice is a combination of vancomycin [1 mg/0.1 ml] and ceftazidime [2 mg/0.1 ml] with or without antifungal agents (amphotericin B, 5–10 μg/0.1 mL, or voriconazole 100 μg/0.1 m).

Vitrectomy has a key role in the treatment of endophthalmitis, as it decreases the pathogen, debris, and inflammatory mediator levels while allowing for a larger sample of the vitreous to be obtained and for the injection of intravitreal antibiotics and/or antifungal agents.

The role of vitrectomy and its timing in endogenous endophthalmitis are less established, as the indications and guidelines formulated from the Endophthalmitis Vitrectomy Study (EVS) relate to exogenous post-cataract endophthalmitis. Vitrectomy is considered mandatory when there is worsening of the signs and/or symptoms after initial treatment, in rapidly progressive cases, retinal necrosis, and extensive subretinal abscess or in the presence of retinal detachment.

Systemic Treatment

Contrary to exogenous endophthalmitis and the guidelines formulated from the EVS, in endogenous endophthalmitis, systemic antimicrobial or antifungal medication has a key role in the treatment of the condition.

Bacterial: A long-term intravenous antibiotic treatment is imperative. Initial dosing and drug selection should be adequate for the treatment of the underlying systemic infections. It is therefore recommended that such treatment should be administered after consultation with infectious disease specialist.

In the absence of systemic diagnosis, broad-spectrum coverage is indicated, usually comprised of vancomycin for gram-positive bacteria and ceftazidime for gram-negative infection.

Fungal: If the patients' history, physical examination, or culture suggests a fungal infection, intravenous treatment with amphotericin B, fluconazole, or the newer caspofungin or micafungin is warranted. Treatment duration and dosing may vary with response to underlying medical conditions. Toxic side effects such as renal and hepatic toxicity mandate consideration while monitoring the ocular and systemic clinical response.

Prognosis

Overall, despite prompt and aggressive treatment, visual prognosis in cases of endogenous endophthalmitis is usually unsatisfactory with

40–50% having a final vision of light perception (LP)/no light perception (NLP).

The prognosis is directly related to the pathogen virulence, the patient's systemic condition, and the extent and location of the ocular infection. A poorer visual prognosis is observed in cases of optic nerve or macular involvement and delayed diagnosis and a better prognosis in cases with more anterior and localized involvement.

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Bacterial Adhesion in Ophthalmology, Characteristics of

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Definition

Ability of bacteria to adhere to biomaterials.

Basic Characteristics

Bacterial adhesion, primarily during the implantation process of ocular implants such as intraocular lenses, is followed by bacterial accumulation. Bacteria replicate, congregate, and form multiple layers of microcolonies embedded in an exopolysaccharide matrix, leading to the formation of a confluent structured biofilm. Implant-related infections such as endophthalmitis after cataract surgery are caused by biofilm. *Staphylococcus epidermidis* is the most common organism responsible for infections of implanted medical devices. Bacterial adhesion depends on the net sum of attractive and repulsive forces generated between the bacterial and substratum surfaces. Among the nonspecific interactions that play a role in primary bacterial adhesion, hydrophilic/hydrophobic interactions are believed to have an important influence. Bacteria, such as *staphylococcus epidermidis*, are mainly negatively charged and show greater adhesion to hydrophobic polymers. Hydrophobic intraocular lens materials such as silicone, polymethyl methacrylate, or hydrophobic acrylic intraocular lenses are more prone to bacterial adhesion than hydrophilic intraocular lenses. Recent epidemiological studies of endophthalmitis rates after cataract surgery with implantation of different intraocular lens materials have shown that implantation of silicone intraocular lenses is associated with increased rates of endophthalmitis as compared to hydrophilic intraocular lenses.

Cross-References

▶ Cataract Surgery
▶ Endophthalmitis
▶ Intraocular Lens

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Bacterial Conjunctivitis

► Haemophilus influenzae, Conjunctivitis

Bacterial Keratitis

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Definition

Infectious keratitis caused by bacteria.

Epidemiology

The reported incidence of post-refractive surgery bacterial keratitis ranges from 0.035% to 1.5%.

Clinical Features

Patients report about decreased vision, foreign body sensation, pain, photophobia, tearing or are asymptomatic. In slit-lamp examination, corneal infiltrates can be identified in the interface (LASIK) or superficial with epithelial involvement (Lasik, surface ablation). Infectious keratitis after refractive surgery has been classified as early onset (occurring within the 1–2 weeks after surgery) or late onset (occurring after 1 or 2 weeks to 3 months after the surgery). While in cases of early-onset bacterial keratitis is often associated with gram-positive bacteria, atypical mycobacteria have been identified in late-onset keratitis.

Tests

Corneal scraping should be done for microbiological analysis (culture, polymerase chain reaction) prior to antibiotic therapy.

Differential Diagnosis

Diffuse lamellar keratitis, viral keratitis, fungal keratitis, parasitic keratitis.

Etiology

In most cases, it is difficult to determine the origin of infection. Bacterial keratitis after refractive surgery is often associated with a compromised epithelial barrier, excessive surgical manipulation, intraoperative contamination, delayed postoperative reepithelialization of the cornea, bandage contact lens, healthcare environment, blepharitis, dry eye, and use of topical corticosteroids. Several sources of infection have been reported and include surgical instruments, surgeons' hands, environmental factors, and periocular flora originating from the eyelids and conjunctiva.

Treatment

Empirical broad-spectrum antibiotic treatment should be started immediately (e.g., combination of vancomycin with either an aminoglycoside or fluoroquinolone) and modified according to microbiological findings. In case of corneal infiltrates in the interface, immediate flap lifting and irrigation with antibiotics should be performed. In severe cases, amputation of a LASIK flap may be necessary.

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Bacterial Keratitis with Ulceration

► Ulcerative Keratitis Disease

Balint Syndrome

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Definition

Balint syndrome (BS) is an uncommon but often debilitating neurological disorder characterized by the triad of simultagnosia, optic ataxia, and ocular apraxia. Simultagnosia is the inability to interpret complex visual displays due to difficulty with processing multiple items (i.e., "missing the forest for the trees"). Patients with simultagnosia have difficulty recognizing more than one object at a time in the presence of multiple distracting objects in the same field. Optic ataxia is an impairment in visuospatial perception where visually guided reaching for objects in space is impaired. Optic apraxia is the poor initiation of conjugate eye movements.

Etiology

BS is usually due to damage to the superior temporal-occipital lobes (Brodmann areas 19 and 7). The "two-stream" hypothesis for higher-order visual processing helps to understand the pathogenesis of BS. In this model, the ventral stream moves from the occipital lobe (i.e., primary visual cortex) through the temporal lobe, and the dorsal ventral stream moves from the occipital lobe through the parietal lobe. Disruption of the dorsal stream typically bilaterally produces the BS. BS can be the result of bilateral ischemic or hemorrhagic strokes, intracranial tumors, traumatic brain injury, and neurodegenerative diseases (e.g., posterior cortical atrophy with Alzheimer's disease).

Diagnosis

BS is a clinical diagnosis supported by characteristic neuroimaging of bilateral occipital-temporal-parietal lobe damage.

Differential Diagnosis

The differential diagnosis of BS includes primary or secondary dementia, psychosis, or cortical blindness.

Clinical

BS can be severely debilitating. Simultagnosia may present with reading difficult despite normal visual acuity and relatively normal comprehensive eye exams. Visuospatial difficulties can manifest as problems walking, eating, and drinking. Patients with optic ataxia may have problems reaching for and grasping objects accurately in their visual field.

Treatment

The treatment of BS should be directed at the underlying etiology. Visual and neurocognitive rehabilitative approaches include adaptive (functional) approaches, focused targeting and other compensatory strategies, and retraining in perceptual skills (e.g., tabletop activities and sensorimotor exercises).

Prognosis

The general prognosis for BS is variable but often poor because most of the etiologies for BS are severe and irreversible (e.g., trauma, stroke, neurodegenerative disease).

Epidemiology

There is no racial predilection for BS but the epidemiology of BS depends in part upon etiology. For example, older age is a risk factor for ischemic stroke or primary neurodegenerative disease (e.g., posterior cortical atrophy) versus younger age in trauma.

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Band Keratopathy

► Calcific Band Keratopathy

Band-Shaped Keratopathy

► Keratinoid (Spheroidal) Degeneration

Band-Shaped Nodular Dystrophy of the Cornea

► Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
► Keratinoid (Spheroidal) Degeneration
► Spheroidal Degeneration

Bardet–Biedl Syndrome, Renal

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Synonyms

BBS; Laurence–Moon–Bardet–Biedl syndrome; Laurence–Moon–Biedl syndrome; Laurence–Moon syndrome; LMBBS; LMS

Definition

Bardet–Biedl syndrome (BBS) is a ciliopathic human genetic disorder that is characterized principally by truncal obesity, rod–cone dystrophy, retinitis pigmentosa, postaxial polydactyly, male hypogonadism, complex female genitourinary malformations, and renal abnormalities and/or failure in some cases.

Etiology

Bardet–Biedl syndrome can result from mutations in at least 14 BBS genes regulating the protein expression for cilia that are involved in cell movement, perception of sensory input, and many different chemical signaling pathways.

Clinical Presentation

The retinal dystrophy appears as an atypical pigmentary retinal dystrophy of the photoreceptors with early macular involvement. One of the major features of Bardet–Biedl syndrome is vision loss from gradual retina deterioration. Problems with night vision become apparent by mid-childhood, followed by blind spots that develop in the peripheral vision enlarging over time and produce tunnel vision. Most people with Bardet–Biedl syndrome also develop poor visual acuity and become legally blind by adolescence or early adulthood.

Cone–rod dystrophy is a form of retinal dysfunction. The photoreceptor cells in the retina gradually deteriorate (cone–rod dystrophy), causing vision loss. Symptoms associated with cone–rod dystrophy may not become apparent until 7 or 8 years of age when an impaired ability to see in dim light or the dark (night blindness) may develop.

The progression and degree of visual impairment varies among affected individuals. In most cases, vision becomes progressively worse through the first and second decade. Affected individuals often experience loss of peripheral vision, a condition sometimes termed tunnel vision. At some point during childhood or adolescence, many affected individuals eventually lose central vision as well, resulting in severe visual impairment or blindness. In some cases, the degeneration of the retina may follow the characteristic course of retinitis pigmentosa, with night blindness, loss of the ability to discriminate color, and progressive tunnel vision.

Additional ocular findings may occur including strabismus, abnormal, nystagmus, cataracts, and glaucoma.

Differential Diagnosis

Kaufman–McKusick syndrome
Typical retinitis pigmentosa

Therapy

Standard of care includes supportive diet intervention as obesity progresses, appropriate HgA1c levels maintained as type 2 diabetes develops, antihypertensive agents protective of renal function, and anticholesterol agents.

Prognosis

Very poor prognosis as end-stage renal failure, and blindness often occurs in Bardet–Biedl syndrome.

Epidemiology

Autosomal recessive disorder displaying pleiotropism and genetic heterogeneity.

In most of North America and Europe, Bardet–Biedl syndrome has a prevalence of 1 in 140,000–1 in 160,000 newborns. The condition is more common on the island of Newfoundland where it affects an estimated 1 in 17,000 newborns. It also occurs more frequently in the Bedouin population of Kuwait, affecting about 1 in 13,500 newborns.

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Bartonella henselae, Cat Scratch

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Synonyms

Bartonella neuroretinitis; Cat scratch disease

Definition

Bartonella henselae is an aerobic intracellular gram-negative bacillus that infects both humans and cats. It is responsible for a broad range of clinical syndromes including optic neuropathy. Bartonella optic neuropathy commonly occurs in the setting of infectious neuroretinitis characterized by optic disk swelling, retinal infiltrates, localized vasculitis, subretinal fluid, and eventually a characteristic macular stellate exudate.

Etiology

Bartonella henselae may be transmitted from its major reservoir of cats to humans via cat scratches, cat bites, or flea bites, leading to infection. In immunocompetent patients, response to the infection tends to be suppurative and granulomatous and is associated with microabscess formation, while in immunocompromised patients the response tends to be vasoproliferative.

Clinical Presentation

There are a variety of clinical presentations associated with *Bartonella henselae* infections. The eye is the most commonly affected nonlymphatic organ in those with *Bartonella henselae* infection, and one of the ocular manifestations is neuroretinitis. Neuroretinitis often presents with a febrile prodromal illness followed by acute painless unilateral visual loss with optic nerve swelling and a macular star figure. Visual acuity at presentation varies and may worsen over the first several days. Optic nerve disc swelling may be seen but the degree of swelling is variable. The disc edema phase followed by subretinal fluid in the macula usually presents before the formation of macular star. Many patients develop macular exudates days after the visual loss leading to a macular star figure that is more prominent in the first 2–3 weeks. Other symptoms and signs that may be present in cat scratch disease include dyschromatopsia, segmental optic neuritis, relative afferent pupillary defect, retinal white dot syndrome, focal choroiditis, and variable visual field defects (cecocentral, central, or arcuate).

Diagnostics

The clinical diagnosis is confirmed by acute and convalescent serology for *Bartonella henselae* IgM and IgG antibodies.

Differential Diagnosis

The most common cause of infectious neuroretinitis is cat scratch disease. Tuberculosis, Lyme disease, syphilis, leptospirosis, toxoplasmosis, viral disease, and toxocariasis are less common infectious etiologies. The clinical presentation however can be mimicked by ischemic optic neuropathy, diabetic papillitis with diabetic exudative retinopathy, hypertensive optic neuropathy with retinovascular disease, papilledema (e.g., pseudotumor cerebri), and sarcoidosis. Although an etiologic diagnosis after can usually be made, many cases of neuroretinitis are idiopathic.

Prophylaxis

Prevention of *Bartonella henselae* infection consists of minimizing the outdoor and free-ranging behavior and flea infestation of domestic cats. Treating infected cats has been controversial in preventing human infection, as recurrent bacteremia is common and force-feeding antibiotics may lead to more scratches and trauma. We do not generally recommend treatment or elimination of the cat. However, disinfecting and washing of any cat scratches or bite wounds may reduce the risk for infection. Immunocompromised patients should definitely avoid scratches and control flea infestation in their cats.

Therapy

Treatment of *Bartonella henselae* infection varies based on clinical manifestation as well as the

immune status of the patient. There is a lack of randomized controlled data in the literature regarding the most effective proven therapy for Bartonella infection. The current treatment for neuroretinitis is based on observational case studies, and doxycycline is one drug used for its ability to produce intraocular and central nervous system penetration. Azithromycin, ciprofloxacin, and other antibiotics have also been used. Erythromycin may be substituted for doxycycline for children younger than 8 years of age in which tooth discoloration is a concern. Some studies have shown that the addition of rifampin may promote disease resolution, improve visual acuity, and decrease optic disc edema and duration of disease. Treatment duration in immunocompetent patients is usually 2–4 weeks, and duration in immunocompromised patients is about 4 months.

Prognosis

The swelling of the optic nerve usually spontaneously resolves in 2–8 weeks, either leaving a mild pallor or recovering to a normal disc appearance. Macular exudates tend to reach prominence over the first 2 or 3 weeks and stabilize for several weeks before they are gradually resorbed. However, even after the resolution of macular exudates, patients may experience mildly decreased visual acuity, abnormal color vision and evoked potentials, residual disc pallor, subnormal contrast sensitivity, retinal pigment changes, and relative afferent pupillary defects.

Epidemiology

Bartonella henselae's major reservoir is in domestic cats and infection spread is via flea transmission. In the USA most cases occur between the months of July and January. Bartonella infection was thought to be mostly a disease of children, but recent studies have suggested that its incidence in adults is higher than previously recognized. However, children and young adults have been reported to have a higher risk for systemic infection. Immunocompromised patients are also at greater risk of infection and systemic dissemination.

Cross-References

▶ Orbital Apex Syndrome in Neuro-Ophthalmology

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Bartonella Neuroretinitis

▶ *Bartonella henselae*, Cat Scratch

Basal Cell Cancer (BCC)

▶ Basal Cell Carcinoma of Eyelid

Basal Cell Carcinoma of Eyelid

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Synonyms

Basal cell cancer (BCC); Basal cell epithelioma

Definition

A skin malignancy that originates from ▶ basal keratinocytes in the top layer of the skin, the ▶ epidermis. BCC is a locally invasive tumor; metastases are rare.

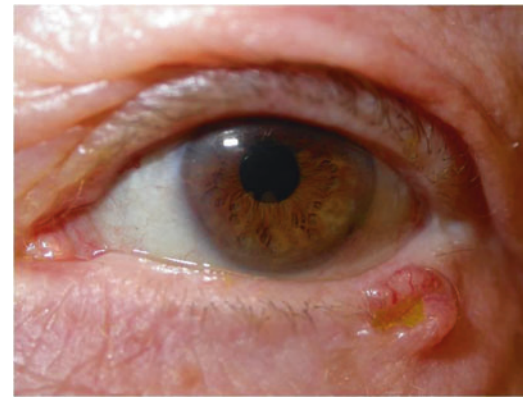
Etiology

Neoplastic transformation of basal cells of the epidermis or infundibular cells of the external root sheath of the hair follicle. Unlike other skin cancers, there are no known precursor lesions to BCC. The risk factors are:

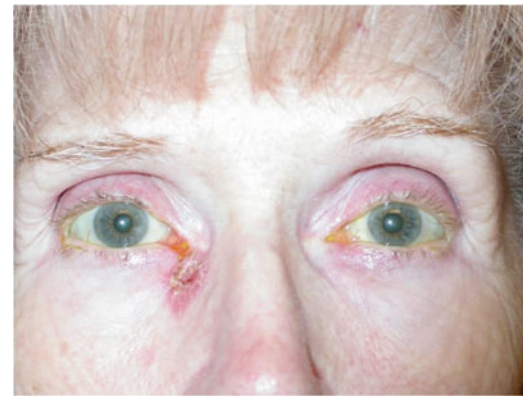
- Ultraviolet light (both UVA and UVB) – chronic sun exposure
- White race (fair skin color, blue-eyed, red or blond hair)
- Geographic location with abundant sun exposure
- Increased age
- Exposure to ionizing radiation
- A history of premalignant ▶ skin lesions or skin cancer
- Genetic disorders such as nevoid basal cell carcinoma syndrome (Gorlin syndrome), ▶ xeroderma pigmentosum, and albinism
- Immunosuppressed states (AIDS or an organ transplant)

Clinical Presentation

Slow growing, locally destructive, and rarely metastasize. May arise anywhere on the eyelid skin, but may be more common on the medial canthus or lower eyelids, where more exposure may occur. Typically, the lesion presents as a firm nodule, raised, rolled, pearly, waxy, or translucent borders with fine telangiectasias and ulcerated or umbilicated center. Other suspicious findings are loss of lashes (madarosis) or eyelid margin notching. Many types of BCC can affect the periocular region, including nodular, nodulouloulcerative, pigmented, cystic, morpheaform, and superficial varieties. The most common form affecting the eyelid is nodular (Fig. 1).



Basal Cell Carcinoma of Eyelid, Fig. 1 Nodulouloulcerative BCC in lower eyelid. Note the loss of cilia on the lower eyelid and telangiectasias of the tumor



Basal Cell Carcinoma of Eyelid, Fig. 2 Morpheaform BCC involving lower eyelid near medial canthus

Morpheaform or infiltrating forms are less common, but more aggressive (Fig. 2). These lesions may be pale, indurated, or patchy. If along the eyelid margin, BCC can mimic blepharoconjunctivitis. The nodular form may be pigmented and confused with ▶ melanoma (Curtis et al. 1993; Albert and Jakobiec 2008; Shields and Shields 2008).

Diagnostics

Clinically by typical appearance and confirmed with ▶ biopsyand histopathologic interpretation.

Differential Diagnosis

Differential Diagnosis includes ▶ keratoacanthoma, ▶ melanocytic nevus, ▶ melanoma, ▶ seborrheic keratosis, ▶ sebaceous carcinoma, ▶ trichoepithelioma, ▶ squamous cell carcinoma, ▶ Bowen disease, and ▶ actinic keratosis.

Prophylaxis

Avoidance of sun and UV exposure (use of sunscreens, sunglasses, umbrellas, and hats).

Therapy

Complete surgical resection with histologic control of margins either by frozen sections or Mohs' micrographic surgery. When surgery is not appropriate or possible, radiotherapy, cryotherapy, or pharmacotherapy can be considered but may be associated with higher recurrence rates than surgical resection.

Prognosis

Depends on the size of the tumor, anatomic location (medial canthus has a worse prognosis), and pattern of infiltrative growth. High cure rates (98%) if early detected and properly treated. However, a tumor recurrence suggests an aggressive propensity.

Epidemiology

In the United States, 380,000–400,000 people each year develop a new BCC. It is the most common malignant tumor of the skin and responsible for 80–90% of malignant eyelid tumors (Curtis et al. 1993; Albert and Jakobiec 2008; Shields and Shields 2008).

Cross-References

- ▶ Actinic Keratosis
- ▶ Bowen's Disease
- ▶ Keratoacanthoma
- ▶ Melanocytic Nevus
- ▶ Melanomas, Conjunctival
- ▶ Sebaceous Carcinoma
- ▶ Seborrheic Keratosis
- ▶ Squamous Cell Carcinoma of Eyelid
- ▶ Trichoepithelioma

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Basal Cell Epithelioma

- ▶ Basal Cell Carcinoma of Eyelid

Basal Cell Nevus Syndrome

- ▶ Basal Cell Nevus Syndrome (Gorlin Syndrome)
- ▶ Gorlin Syndrome

Basal Cell Nevus Syndrome (Gorlin Syndrome)

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Synonyms

Basal cell nevus syndrome; Gorlin syndrome; Nevoid basal cell carcinoma syndrome

Definition

A rare autosomal dominant disorder characterized by multiple nevoid basal cell carcinomas early in life. It is a multisystemic disease involving multiple organ systems.

Etiology

Tumors are indistinguishable from noninherited forms of basal cell carcinoma, arising from the basal cell layer of the epithelium. The gene thought to be responsible for Gorlin syndrome is the patched gene (PTCH), found on 9q22.3-q31. It is thought to be a tumor suppressor with one germ line defect in affected families. Complete penetrance with variable expressivity is observed (Gorlin 1995; Bale 1997; Shields and Shields 1999; Albert and Jakobiec 2008).

Clinical Presentation

Gorlin syndrome may present with multiple basal cell carcinomas at a young age. Eyelid basal cell carcinomas occur in 25% of cases and are indistinguishable from noninherited forms of basal cell carcinoma.

Other ophthalmic findings in Gorlin syndrome include congenital cataracts, orbital cysts, hypertelorism, colobomas, and medullated nerve fiber layer of the retina. Other features include mandibular cysts, macrocephaly, frontal bossing, polydactyly, palmar or plantar pits, and medulloblastoma (Gorlin 1995; Shields and Shields 1999; Albert and Jakobiec 2008).

Diagnostics

Excisional biopsies of suspect lesions are histologically indistinguishable from basal cell carcinoma. Imaging is necessary when clinically correlated, including MRI of the brain, dental radiography, and a skeletal survey.

Differential Diagnosis

Xeroderma pigmentosa

Prophylaxis

Patients with Gorlin syndrome may be extremely susceptible to ionizing radiation and sun exposure. Patient should be counseled to avoid sun exposure.

Therapy

Surgical excision is recommended for a patient with a limited number of lesions. Topical 5-fluorouracil with or without topical tretinoin may be useful for patients with extensive lesions. Oral isotretinoin may be an option for patients who are at high risk for developing many additional lesions.

Prognosis

Patients may have multiorgan involvement and will need care by appropriate specialists, including dermatologists, dentists, oncologists, cardiologists, and orthopedic surgeons.

Epidemiology

Incidence is rare and occurring in about 1 per 50,000–150,000 people and in 0.7 % of patients with basal cell carcinoma. Fair-skinned patients with substantial sun exposure may be more susceptible (Gorlin 1995; Shields and Shields 1999; Albert and Jakobiec 2008).

Cross-References

▶ Basal Cell Carcinoma of Eyelid

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Basal Keratinocytes

► Keratinocytes: Overview

Basosquamous Cell Acanthoma

► Inverted Follicular Keratosis

Batten Disease

► Ceroid Lipofuscinosis

Battle Sign, Facial Nerve Palsy

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Definition

Battle sign, also called mastoid ecchymosis, consists of subcutaneous blood/bruising over the mastoid process of the skull. It can be an indication of fracture in the posterior cranial fossa of the skull, and the finding is a result of extravasation of blood along the path of the posterior auricular artery, which runs vertically and posterior to the external ear. Most posterior cranial fossa fractures occur following lateral and/or posterior blow to the occiput. Posterior fossa fractures can cause injury to the facial nerve, resulting in ipsilateral facial paralysis.

Clinical

Patients with the Battle sign can also present with other signs or symptoms of skull base fracture such as periorbital ecchymosis (i.e., raccoon eyes), cerebrospinal fluid (CSF) rhinorrhea (usually more indicative of an anterior skull fracture), cranial nerve palsy, bleeding from the nose or ears, hemotympanum, hearing loss, nystagmus, vomiting, and optic nerve compression.

The pattern of cranial nerve involvement will depend on the specific location of the fracture. Facial nerve injuries due to longitudinal fractures most commonly occur at the level of the geniculate ganglion, which is located within the facial canal near the middle and inner ear. Fractures through the jugular foramen can also disrupt function of the glossopharyngeal, vagal, and spinal accessory nerves.

Diagnosis

Clinically, patients with lower cranial neuropathies after trauma with or without the Battle sign should be evaluated for a skull base fracture. These skull base fractures are radiographically detected with skull x-rays or more commonly computed tomography (CT) imaging, although if small may be difficult to detect.

Differential Diagnosis

Battle sign can be confused with an expanding hematoma caused by fracture of the mandibular condyle.

Treatment

Skull base fractures may require surgical repair especially if there is associated intracranial injury requiring decompression, persistent cerebrospinal fluid (CSF) leak, or significant cranial nerve or vascular injury.

Prognosis

Prognosis depends on the severity of the trauma and the extent of damage to the cranial nerves. Full recovery is possible depending on severity and rapidity of appropriate evaluation and treatment.

Further Reading

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Bayer

► Aspirin (for Carotid Artery Disease)

Baylisascaris procyonis (Raccoon Ascarid), Diffuse Unilateral Subacute Neuroretinitis

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Synonyms

DUSN

Definition

Diffuse unilateral subacute neuroretinitis (DUSN), previously known as "unilateral wipeout syndrome," was first termed by J. Donald M. Gass in 1978 (Gass and Scelfo 1978). The syndrome refers to a unilateral, potentially blinding, inflammatory disease characterized by mild to severe vitritis, deep white retinal lesions, marked diffuse retinal pigment epithelium changes, and eventual optic atrophy in the late stages, caused by a parasitic infection (Arevalo et al. 2013).

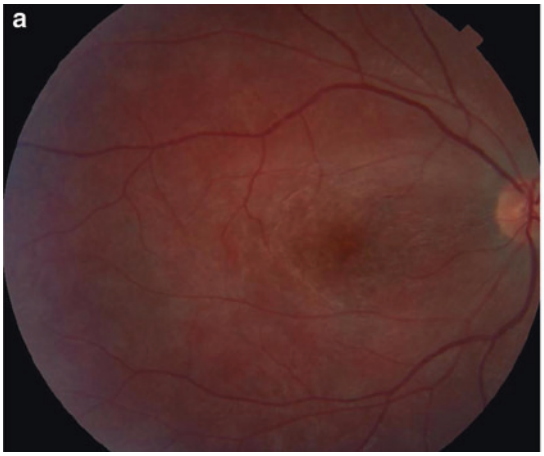
Etiology

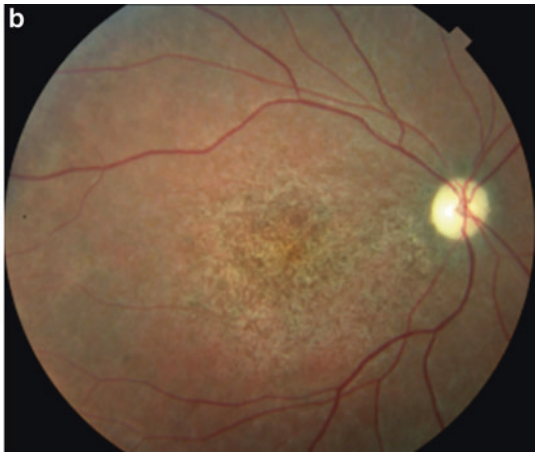
Nematodes of varying sizes have been reported in association with diffuse unilateral subacute neuroretinitis. Although no nematodes have ever been identified, *Baylisascaris procyonis*, also known as the "Raccoon roundworm," is thought to be the larger-sized nematode (1,500–2,000 μm) often isolated in north Midwestern United States, and *Ancylostoma caninum* is thought to be the smaller-sized (400–700 μm) nematode often isolated in Southeastern United States.

Clinical Features

The diagnosis can be obvious with clinical visualization of a subretinal, motile nematode; however, more often the diagnosis is challenging and presumptive when no nematode can be found. DUSN is most frequently seen in healthy children or young adults with no significant ocular or systemic illness. Common ocular symptoms include unilateral paracentral scotoma and blurring of vision.

Early recognition of DUSN is important since prompt removal and destruction of the causative nematode may prevent progressive visual loss. Unfortunately, clinical manifestations of DUSN in the early stages of the disease such as vitritis, deep white retinal lesions, and optic disc swelling may be easily mistaken as multifocal choroiditis, multiple evanescent white dot syndrome, or



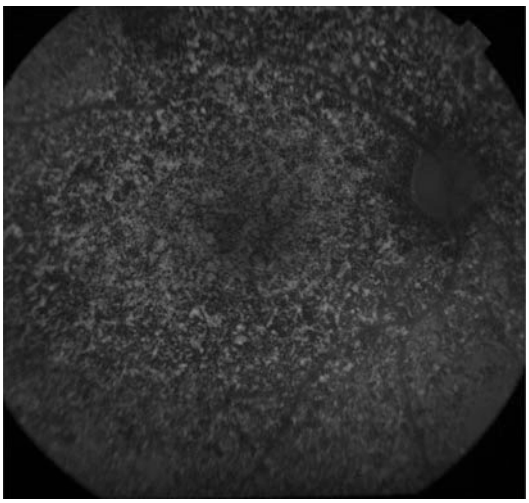


***Baylisascaris procyonis* (Raccoon Ascarid), Diffuse Unilateral Subacute Neuroretinitis, Fig. 1** Color fundus photograph of diffuse unilateral subacute neuroretinitis at presentation and 1 month after. **a** Color fundus photograph at presentation showing nonspecific retinal pigment epithelial changes at the central macula. Note the relatively normal appearing optic disk at this stage. **b** Color fundus photography of the same eye taken 1 month later showing diffuse retinal pigment epithelial changes and severe optic atrophy (Images courtesy of Dr K. Bailey Freund, Vitreous-Retina-Macula Consultants of New York, New York, USA)

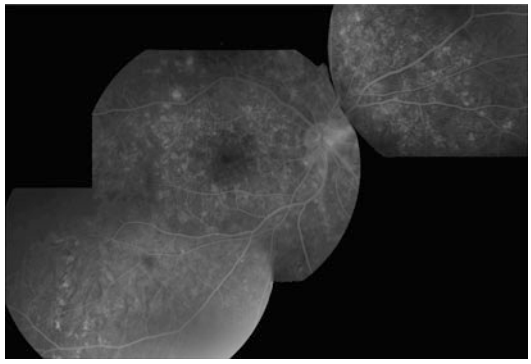
nonspecific optic neuritis and papillitis (Sabrosa and de Souza 2001).

In the early stages, focal retinal pigment epithelial (RPE) changes may be explained by the travel pattern of the worm, while diffuse RPE changes may be explained by a toxic reaction. The focal chorioretinal white spots may be an immune response to the secretion or excretion of the nematode. These lesions may disappear in 1–2 weeks as the nematode moves elsewhere in the eye. In the late stages, retinal arteriolar attenuation, diffuse atrophic changes in the retinal pigment epithelium, and optic atrophy may develop, resulting in irreversible profound vision loss. Choroidal neovascularization may occur as a complication due to breaks in Bruch's membrane presumably created by the movement of the nematode (Gass and Olsen 2001).

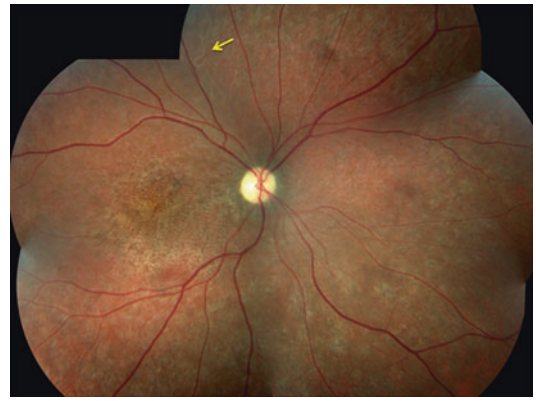
The progression of this disease from its early to late stage can be impressively rapid. In the early stage, there may be nonspecific RPE changes and gray-white retinal lesions, with a relatively normal appearing optic disk. Within a short duration, as short as 1 month, there may be progression to widespread RPE atrophy and optic atrophy (Fig. 1). The extensive involvement of the retina may be rather impressive as evident with fundus autofluorescence (Fig. 2)



***Baylisascaris procyonis* (Raccoon Ascarid), Diffuse Unilateral Subacute Neuroretinitis, Fig. 2** Fundus autofluorescence of diffuse unilateral subacute neuroretinitis showing widespread retinal pigment epithelial changes (Image courtesy of Dr K. Bailey Freund, Vitreous-Retina-Macula Consultants of New York, New York, USA)



***Baylisascaris procyonis* (Raccoon Ascarid), Diffuse Unilateral Subacute Neuroretinitis, Fig. 3** Fluorescein angiographic montage of diffuse unilateral subacute neuroretinitis showing widespread retinal pigment epithelial changes (Image courtesy of Dr K. Bailey Freund, Vitreous-Retina-Macula Consultants of New York, New York, USA)



***Baylisascaris procyonis* (Raccoon Ascarid), Diffuse Unilateral Subacute Neuroretinitis, Fig. 4** Color fundus montage of diffuse unilateral subacute neuroretinitis with a visible nematode in the peripheral retina superiorly (*arrow*) (Image courtesy of Dr K. Bailey Freund, Vitreous-Retina-Macula Consultants of New York, New York, USA)

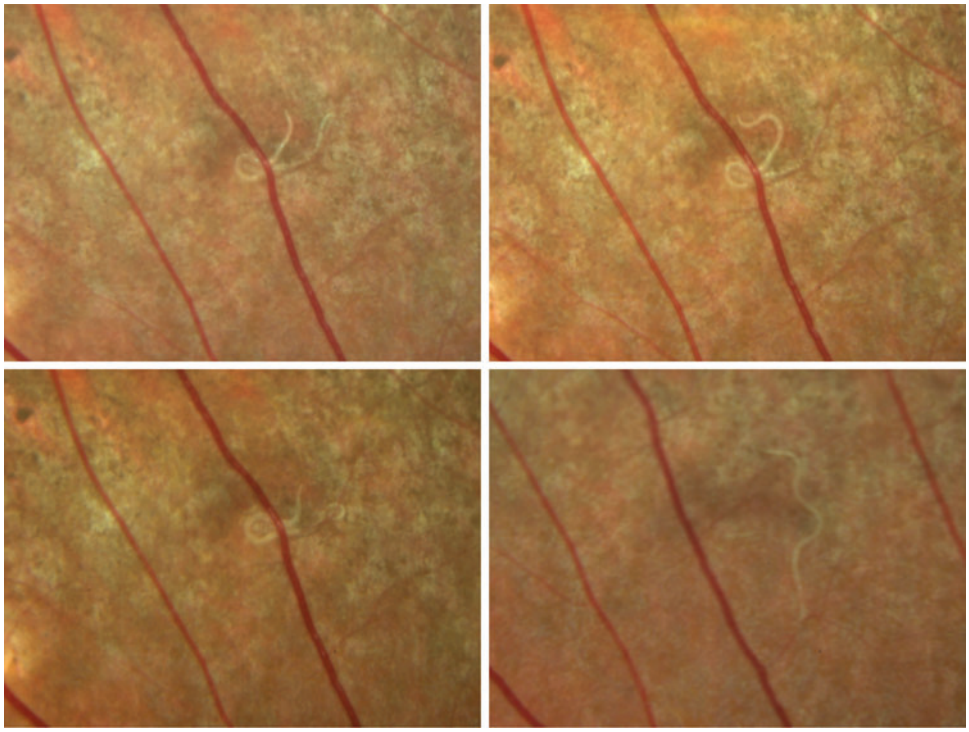
and fluorescein angiogram (Fig. 3). The diagnosis is usually made with documentation of the intraocular nematode with the aid of ultrawide field or montage color photography (Fig. 4) and serial photographs, which demonstrate the motility of the intraocular nematode (Fig. 5).

Diagnostics

Identification of the intraocular nematode requires meticulous examination of the entire retina. In many cases, the intraocular nematode is so minute that it can be easily overlooked. As mentioned, serial fundus photography documenting nematode motility is often the most useful diagnostic test (Fig. 5). Fundus autofluorescence shows widespread hypofluorescent granularity due to RPE abnormalities (Fig. 2). Fluorescein angiography in the early phase may show hypofluorescence of the retinal lesions followed by late staining and leakage of dye from the optic nerve capillaries or peripheral venules. In the later phase, there may be widespread hyperfluorescent window defects from retinal pigment epithelial damage (Fig. 3). Indocyanine green angiography shows hypofluorescent dark spots in the early phase that either disappear or persist in the late phase, indicative of choroidal infiltration. Optical coherence tomography may show a decrease in retinal nerve fiber layer thickness. Visual field studies are nonspecific but may be useful for evaluating visual field before and after treatment. Electroretinography may be highly variable including mild to moderate decrease in rod and cone function and in more severe cases with ischemic retina, a negative electroretinogram. Multifocal electroretinography may show decreased foveal responses, which may improve following treatment. Systemic investigations including serology are often unrevealing unless eosinophilia is present.

Differential Diagnosis

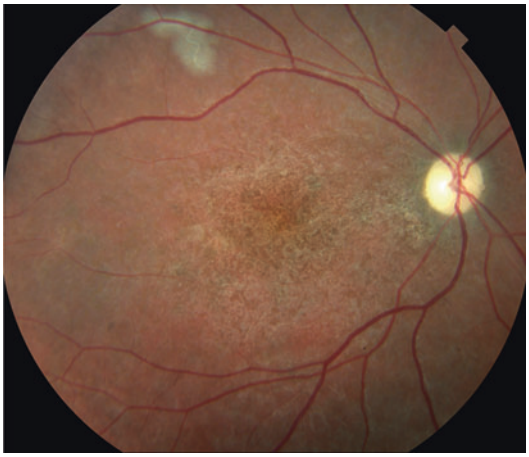
Differential diagnosis of DUSN includes vitritis, multifocal choroiditis, multiple evanescent white dot syndrome, or nonspecific optic neuritis and papillitis.



***Baylisascaris procyonis* (Raccoon Ascarid), Diffuse Unilateral Subacute Neuroretinitis, Fig. 5** Serial color fundus photographs of diffuse unilateral subacute neuroretinitis showing the motility of the nematode (Image courtesy of Dr K. Bailey Freund, Vitreous-Retina-Macula Consultants of New York, New York, USA)

Treatment

The best treatment option of a visible worm is laser photocoagulation as it presumably kills the intraocular nematode as evident by its lack of motility, without causing significant intraocular inflammation. Pretreatment immunosuppression with corticosteroids may reduce retinal inflammation if any. After laser photocoagulation, there may be improvement in vision and resolution of the active vitritis and chorioretinitis. Laser photocoagulation should be aimed at achieving white burns surrounding the nematode (Fig. 6) (Garcia et al. 2004). Other treatment options including oral antihelminthic therapy such as albendazole and pars plana vitrectomy have been tried with variable success. It may be reasonable to treat the patient with 400 mg of albendazole for 30 days if there is any suspicion of systemic involvement.



***Baylisascaris procyonis* (Raccoon Ascarid), Diffuse Unilateral Subacute Neuroretinitis, Fig. 6** Color fundus photograph of diffuse unilateral subacute neuroretinitis after treatment with laser photocoagulation to the nematode (Image courtesy of Dr K. Bailey Freund, Vitreous-Retina Macula Consultants of New York, New York, USA)

Surgical extraction of the nematode using vitrectomy may be difficult in view of the small size and motility of the intraocular nematode, however may be considered if there are any relative contraindications to laser photocoagulation such as if the patient is uncooperative to laser treatment or if the nematode is situated near the posterior pole or macula.

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BBS

▶ Bardet–Biedl Syndrome, Renal

BCD

▶ Bietti Crystalline Retinopathy

Bell Palsy

▶ Seventh Nerve Palsy

Bell's Palsy

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Synonyms

CN VII palsy; Idiopathic facial palsy; Idiopathic facial paralysis

Definition

A Bell palsy is characterized by sudden onset of unilateral, lower motor neuron weakness of CN VII (the facial nerve).

Etiology

The etiology of Bell palsy remains largely unknown, but it is believed to originate from a viral infection, likely herpes simplex, in at least

some of the cases. A certain subset of patients may be at an increased risk for developing Bell palsy; this includes those with diabetes or multiple sclerosis and those that are currently pregnant. While the exact cause remains unknown, the signs and symptoms of Bell palsy are caused by a peripheral lesion to CN VII (the facial nerve) which involves all of its distal branches.

Clinical Presentation

The main characteristic of Bell palsy is unilateral facial weakness which involves the forehead. Although facial weakness on both sides is a rare presentation, this does not completely rule out Bell palsy as a diagnosis. Full facial nerve weakness is usually reached within a few days from the onset of symptoms. Other symptoms may be seen on the same side as the facial weakness and include sensitivity to loud sound (hyperacusis), impaired tear production, subjective mild numb sensation or pain of the ear, tongue, or face, changes in taste and reduced secretion of saliva. Just over half of those with Bell palsy will present with a viral prodrome as well which may include fever, malaise, tingling, or itching of skin over the area to be affected.

Diagnostics

A clinician diagnoses Bell palsy from the patient's history, including time of onset, associated symptoms and precipitating factors, and physical exam findings such as weakness of the muscles of facial expression and the extent of involvement. The diagnosis is made largely by exclusion of other causes. When evaluating a patient for facial paralysis it is important to determine whether the lesion is central or peripheral before doing anything else. This is easily done by asking the patient to raise their eyebrows, if the forehead fails to contract then a peripheral palsy (like Bell palsy) is likely, but if the forehead is able to contract then a central VII nerve palsy is more likely and the patient should be evaluated for a possible cerebral vascular accident. There are no laboratory or imaging tests used to definitively diagnose Bell palsy.

Differential Diagnosis

Cerebral vascular accident, Möbius syndrome, facial colliculus syndrome, acoustic neuroma, Lyme disease, sarcoidosis, metastatic lesions, temporal bone fracture, Ramsay Hunt syndrome, otitis media, congenital facial palsy, Guillain-Barré syndrome, and hemangioma.

Prophylaxis

There is no known prophylactic treatment for this condition.

Therapy

Due to the idiopathic nature of the disease, treatment for Bell palsy is controversial and limited. Most patients will recover spontaneously within a few weeks even without treatment. Corticosteroids such as prednisone have been reported to speed the recovery of Bell palsy. High quality evidence, however, has shown no significant benefit from anti-herpes simplex antivirals compared with placebo in producing complete recovery from Bell palsy, and lesser quality evidence has suggested that antivirals were significantly less likely than corticosteroids to produce complete recovery.

For patients that are not able to close their eyelid due to the paralysis, artificial tears or ointment should be used to prevent drying of the eye and related ophthalmic complications.

Prognosis

In general, the prognosis for those with Bell palsy is excellent. Most patients begin to recover within

3 weeks from the onset of their symptoms, and the remainder will show improvement within 3–6 months. Most individuals can expect to recover full function of the facial nerve, but some will have residual weakness. Although all patients will show some improvement in their symptoms, a very small subset will have poor return of function. Those that begin to recover sooner generally have the best chances of regaining full function. Patients that experience hyperacusis or decreased tear production, are after over 60 years of age, or suffer from diabetes, hypertension, or a psychiatric disease have a poorer prognosis. Once a patient has made a full recovery, they do not typically experience any adverse sequelae. Recurrence is seen in less than 20% of cases.

Epidemiology

The annual incidence of Bell palsy is approximately 20–25 per 100,000 individuals. It occurs equally in both genders and among races. There is an increasing incidence with increasing age. A small percentage of those affected have a history of prior facial palsy or have a family history of Bell palsy. Geographic location does not have any influence on the prevalence of this condition. Paralysis of the facial nerve occurs equally on the left as the right. Those that are pregnant or have a history of diabetes or multiple sclerosis may be at an increased risk to develop Bell palsy.

Cross-References

► CN VII Palsy

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Benign Anisocoria

► Physiologic Anisocoria

Benign Episodic Pupillary Mydriasis

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Synonyms

Benign episodic unilateral mydriasis; Episodic anisocoria; Migraine with benign episodic unilateral mydriasis; Springing pupil; Transient benign unilateral pupillary dilation

Definition

Benign episodic unilateral mydriasis (BEUM) or benign episodic pupillary dilation (BEPD) is an isolated benign cause of intermittent transient pupil asymmetry. It comprises a heterogeneous set of conditions. BEPD usually affects young,

healthy women but can occur in any age and in any gender. It has a benign prognosis and does not necessitate further workup.

Etiology

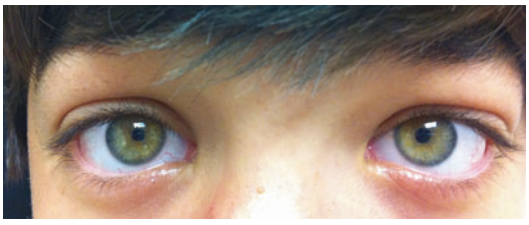
The exact pathophysiology for BEPD is unclear. It had been hypothesized that alterations in the interplay between the sympathetic and parasympathetic activity of the iris (e.g., parasympathetic insufficiency of the iris sphincter in some cases, or sympathetic hyperactivity of the iris dilator in others).

Clinical Presentation

Typically patients present with transient BEPD, and each episode may last from minutes to hours is self-limited, and spontaneously resolves. BEPD can be seen in patients with the history of headache; however, it has also been described without accompanying headache. The association with BEPD and migraine had been reported in the literature, and some authors consider it to be a limited form of ophthalmoplegic migraine. BEPD may be associated with blurring of vision, periocular pain, and photosensitivity; however, it has not been reported to be associated with any systemic or neurologic disease. The only ocular finding during the event is pupil asymmetry (anisocoria) (see Fig. 1).

Diagnostics

A detailed medical history including medications and physical examination, including ophthalmic and neurological evaluation, is crucial in the diagnosis of BEPD. BEPD appears to have a benign neurological prognosis and does not require further neurodiagnostic studies.



Benign Episodic Pupillary Mydriasis, Fig. 1 Minimal Mydriasis seen in left eye.

Differential Diagnosis

- Physiologic anisocoria
- Mydriasis secondary medication side effect
- Adie's tonic pupil
- Intermittent angle-closure glaucoma
- Partial third nerve palsy
- Posterior cerebral artery aneurysm
- Tentorial herniation
- Horner syndrome
- Traumatic mydriasis

Therapy

Patient education and reassurance are typically all that is necessary for BEPD.

Cross-References

- ▶ Adie's Tonic Pupil
- ▶ Horner Syndrome
- ▶ Third Nerve Palsy

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Benign Episodic Unilateral Mydriasis

▶ Benign Episodic Pupillary Mydriasis

Benign Epithelial Melanosis

▶ Ephelis (Freckle), Conjunctival Disease

Benign Essential Blepharospasm: Orbital and Oculoplastic Considerations

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Definition

Benign essential blepharospasm is a form of focal dystonia which involves involuntary contraction of the orbicularis oculi, resulting in uncontrollable eyelid twitching (Anderson et al. 1998). Meige's syndrome is a combination of blepharospasm and oromandibular dystonia, the latter of which is described by a constellation of symptoms including marked difficulty opening or closing the jaw, lateral jaw deviation, teeth grinding, and jaw pain (Jankovic 1988).

Etiology

The etiology of benign essential blepharospasm and Meige's syndrome is not entirely understood. Formerly thought of as a predominately psychological condition, evidence from advances in neuroimaging and research techniques support potential neurolopathologic etiologies (Hallet 2002). Eyelid blinking is normally an involuntary response involving sophisticated neuronal circuitry, including cranial nerves 2 (afferent), 5 (afferent), and 7 (efferent) (Ben Simon and McCann 2005). A central area that coordinates eyelid blinking is thought to inhabit deep cerebral structures, such as the basal ganglia and/or brain stem. A single causative factor has not yet been identified in the pathophysiology of blepharospasm. Given the complex neuroanatomy underlying this disorder, the etiology is likely to be as complex (Jankovic 1988; Hallet 2002; Ben Simon and McCann 2005).

Epidemiology

Blepharospasm is an uncommon disorder that is frequently misdiagnosed. The prevalence of blepharospasm is estimated to be approximately 1 in 20,000 with a female predominance of nearly 2:1. Average age of onset is in the mid-50s, with most patients older than 60 (Anderson et al. 1998).

Clinical Presentation

Benign essential blepharospasm may go mis- or undiagnosed for a prolonged period of time. Eyelid twitching may be ignored by the patient until it worsens to a point where they seek medical attention. Physicians unfamiliar with this condition may underestimate a patient's complaints or prescribe ineffective treatments such as artificial tears or sunglasses (Anderson et al. 1998; Ben Simon and McCann 2005).

Patients complain of involuntary, painless, episodic eyelid twitching or closing that is usually bilateral. In severe episodes, patients cannot open their eyes at all. Spasms can be provoked or unprovoked and often worsen as the patient ages. Patients may also complain of dry eyes, allergic symptoms, photophobia, and eye strain with reading or watching television (Jankovic 1988; Anderson et al. 1998). These symptoms can cause marked emotional distress and can lead to social embarrassment and even withdrawal. Patients with Meige's syndrome present with multiple jaw-related complaints in addition to blepharospasm (Jankovic 1988).

Diagnosis

Oftentimes, benign essential blepharospasm or Meige's syndrome can be diagnosed in the office based on direct observation of the spasms. As

these conditions generally worsen with time, blepharospasm is often quite apparent by the time patients seek medical attention. Other times when blepharospasm is not apparent in the office, the physician must rely solely upon history or ask patients to videotape episodes (Jankovic 1988; Defazion and Livrea 2004).

When considering the diagnosis of benign essential blepharospasm or Meige's syndrome, it is important to rule out secondary causes of blepharospasm. The most common cause of reflexive blepharospasm is dry eye and other ocular surface abnormalities (Ben Simon and McCann 2005). Other causes of secondary blepharospasm include ocular inflammatory disorders, seizure activity, meningeal irritation, and brain stem abnormalities (vascular insufficiency, space occupying lesion, etc.).

In benign essential blepharospasm or Meige's syndrome, treatments for coincidental dry eye or ocular inflammation are not impressive. Serologic investigations and standard neuroimaging studies do not reveal a causative factor (Anderson et al. 1998).

Differential Diagnosis

Bell's palsy
Cerebral vascular accident
Cerebral space occupying lesion
Drugs (antipsychotics, cholinergics, cocaine)
Dry eye
Eyelid myokymia
Hemifacial spasm
Meningeal irritation
Intra- and extraocular inflammation
Seizure

Treatment

There is no cure for benign essential blepharospasm and Meige's syndrome. Treatment anchors on temporally alleviating spasmodic episodes and begins with identifying and treating any afferent-arc-related issues that may be exacerbating the condition. This includes artificial tears for dry eye, lid hygiene for blepharitis and meibomian gland dysfunction, and sunglasses for photophobia. Benzodiazepines have been reported to provide temporary relief, but effectiveness cannot be predicted (Anderson et al. 1998).

Serial injections of Botulinum A toxin is considered by most physicians to be the most effective treatment for blepharospasm (Anderson et al. 1998; Defazion and Livrea 2004). Botulinum A toxin prevents the exocytosis of presynaptic vesicles containing acetylcholine, which decreases the concentration of acetylcholine in the motor end plate, resulting in paralysis of skeletal muscles. Patients begin to experience relief within 1 week and the effect lasts a mean of 3–5 months. Treatment can be repeated and adjusted to optimize results based on previous treatments.

There are more invasive surgical options for blepharospasm when medical options fail. One very effective option is the protractor myectomy procedure (Gillum and Anderson 1981). In this procedure, much of the orbicularis oculi muscle and the corrugator supercilii muscle are extirpated from the eyelid. Other alternative treatments include proximal and distal facial neurectomy and the superior cervical ganglion block (Ben Simon and McCann 2005).

Prognosis

For most patients, the prognosis is good. Once the condition is diagnosed, customized treatment alleviates blepharospasm in over 95% of patients (Anderson et al. 1998).

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Benign Essential Blepharospasm: Neuro-ophthalmic Considerations

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Synonyms

Blepharospasm; Focal dystonia; Spasm of eyelids

Definition

BEB is an uncommon neurological disorder that causes an involuntary, intermittent muscle spasms and contractions of the facial muscles around the eyes bilaterally. Symptoms can range from mild intermittent eyelid twitching to excessive blinking and sometimes constant or debilitating persistent spasm and closure of the eyes. There is no clear cause but is believed to be a form of localized dystonia.

Etiology

Although BEB was thought to be a psychological disorder in the past, most authors now believe that BEB is multifactorial in origin. Some have postulated a defect in the control circuits in the basal ganglia, midbrain, and brain stem that regulate and coordinate the normal eyelid and blinking activities. Several studies have shown decreased corneal sensitivity, and a relationship to impaired cortical processing of sensory input and secondary loss of the inhibition of the blink reflex as a mechanism has been proposed. The efferent (motor) pathway for eyelid closure primarily includes the facial nerve and its innervation to the orbicularis oculi, corrugator, and procerus muscles.

Clinical Presentation

Patients with BEB may complain of tearing, eye irritation, photophobia, and vague ocular pain before or during the spasm episodes. In the early stages, BEB is typically characterized by intermittent forced blinking (77%) and subjective eye irritation (55%) that can be triggered by different stimuli (e.g., bright lights, emotional stress or tension, fatigue, wind, or air pollution). BEB in contrast to hemifacial spasm is bilateral. The muscle spasms (66%) and contractions symptoms often increase gradually and in severe cases BEB may progress to a continuous or disabling cycle leading to functional blindness. Usually BEB symptoms occur during the day while awake and disappear while sleeping. BEB symptoms may be temporarily relieved by sleep (75%), relaxation (55%), inferior gaze (27%), artificial tears (24%), talking (22%), eyelid traction (22%), singing (20%), and humming (19%). Although BEB is typically an isolated disorder, it may be associated with dystonia of the face, mouth, or jaw. BEB may also be associated with or triggered by dry eyes (49%). The vast majority of BEB is neurologically isolated, but rare cases are due to underlying neurological disease (8%). Patients with BEB may also have apraxia of eyelid opening (AELO) characterized by a temporary inability to open the lids voluntarily. Some patients develop a "sensory trick" to help them to open the lids. Typically, once the lids open either spontaneously or with manual elevation, they remain open in AELO.

Diagnostics

The diagnosis of BEB is a clinical diagnosis, and there is no diagnostic laboratory or radiographic finding.

Differential Diagnosis

1. Meige syndrome
2. Apraxia of lid opening
3. Myokymia
4. Fasciculation
5. Hemifacial spasm
6. Dystonia
7. Bell's palsy

Prophylaxis

Non-applicable.

Therapy

Although no cure currently exists, patients have different options for treatment. The first line of treatment measures includes reducing the environmental and other triggers, using tinted sunglasses or specific filters to reduce painful light sensitivity (photo-oculodynia), lid hygiene to decrease irritation and any concomitant blepharitis, and treatment of dry eyes (e.g., artificial tears, topical drops, punctal occlusion).

Pharmacotherapy includes an extensive list of drugs that have been used to treat BEB; however, they have partial and transient relief (e.g., lorazepam, clonazepam, and Artane). Local injection of botulinum A toxin is considered the most effective (95%) treatment of choice for BEB. Botulinum toxin interferes with acetylcholine release from the nerve terminals, leading to a temporary paralysis of muscles. The paralytic effect is dose related, and the peak effect is at 5–7 days after injection with a mean duration of action of 3 months. Complications of botulinum toxin injections include ptosis, diplopia, corneal exposure, dry eye, entropion, ectropion, epiphora, photophobia, and ecchymosis.

Surgical treatment of BEB is reserved for patients who fail maximal medical therapy and includes myectomy and frontalis suspension. One other treatment modality that has shown some anecdotal benefit in the treatment of BEB is superior cervical ganglion block.

Prognosis

The prognosis of BEB is variable and the severity ranges from mild to debilitating.

Epidemiology

There are up to 2,000 new BEB cases diagnosed annually with a prevalence of approximately 5 in 100,000 of the general population. There are up to 50,000 cases of BEB in the United States. It's preponderance in female with female to male ratio of 1.8:1. The mean age of onset is 56 years, with around two thirds of patients 60 years or older.

Cross-References

► Apraxia of Lid Opening

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Benign Intracranial Hypertension

▶ Idiopathic Intracranial Hypertension

Bergmeister's Papilla

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Synonyms

Persistent hyaloid artery

Definition

Connective tissue on the disc associated with an avascular prepapillary membrane or veil. It is the result of incomplete resorption of the hyaloid artery before birth.

Cross-References

▶ Persistent Hyaloid Artery
▶ Persistent Pupillary Membrane
▶ Persistent Tunica Vasculosa Lentis

Berlin's Edema

▶ Commotio Retinae (Berlin Disease/Edema)

Best Disease

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Synonyms

Best vitelliform macular dystrophy; Vitelliform macular dystrophy; Vitelliform macular dystrophy type 2

Definition

Best disease is an autosomal dominantly inherited bilateral disorder of variable penetrance and expressivity characterized by variable deposition of yellow yolk-like macular cysts, good visual acuity, subnormal electrooculogram (EOG), and progression throughout life.

Etiology

Best disease is caused by mutations in the VMD2 gene on chromosome 11q13 that codes for bestrophin-1, a calcium-sensitive chloride (Cl^-) channel protein that is found on retinal pigment epithelial (RPE) cells. Disease-causing mutations in bestrophin-1 protein result in defective Cl^- channel conductance. Abnormalities in EOG are thought to be a result of this defective Cl^- conductance. The yolk-like yellow macular lesions characteristic of the vitelliform stage of Best disease are thought to be due to abnormal accumulations of lipofuscin and possibly unphagocytized outer photoreceptor segments in the RPE and subretinal space.

Clinical Presentation

Most vitelliform lesions are found on routine exam. Visual acuity is often only minimally affected, although poor vision is possible, especially in older patients. Findings are usually bilateral; however, unilateral changes have been reported. For most patients, there is a very gradual progressive vision loss. Carriers of Best disease usually have no fundus findings.

Several clinical stages exist with Best disease. These are summarized in Table 1. Although vitelliform lesions have been reported as early as the first week of life, patients usually have a normal appearing fundus during the first few months to years of life. Typically, the vitelliform stage occurs between 3 and 15 years of age. A central, round or oral, sharply circumscribed subretinal yellow cyst that resembles a yolk of a sunny-side up egg is the classic vitelliform lesion. This lesion usually measures 1/2 to 2 disk diameters in size and is uniform in color. Sometimes multiple vitelliform cysts may occur.

Best Disease, Table 1 Clinical stages of best disease

Clinical stage	Description
Normal fundus	Normal fovea but abnormal EOG
Previtelliform	RPE defects, small round yellowish dot in foveola or tiny honeycomb-like structure centrally
Vitelliform	Round or oval, sharply circumscribed, smooth macular subretinal lesion uniformly filled with yellow material of ½ to 2 disk diameters in size with appearance similar to yolk of an egg
Scrambled egg	Yellowish material begins to disintegrate with borders of lesion becoming more irregular and less discrete. Visual acuity ranges from 20/30 to 20/40
Pseudohypopyon or cystic phase	Yellowish material disintegrates and layers in the lower half of cyst, resembling a hypopyon
Round chorioretinal atrophy stage	Macula becomes atrophic. Subretinal fibrous scar formation can occur. Patients may develop choroidal neovascularization. Visual acuity usually 20/100 or less

With time, the yellowish material within the lesion may begin to disintegrate, making the "yolk" appear more like "scrambled eggs." This change is usually accompanied by a decrease in visual acuity to about the 20/40 level. Occurring often in puberty, the yellowish material may also layer in the inferior half of the lesion. The lesion appears to have a fluid layer similar in appearance to a hypopyon, so this stage is sometimes referred to as the pseudohypopyon stage.

With time, the yellowish material may disappear and the retina becomes atrophic, resulting in decreased vision to the 20/100 or worse range. Pigment hyperplasia can also occur. Occasionally a fibrous subretinal scar may develop. Choroidal neovascularization can occur with these lesions.

Diagnosis

Diagnosis of Best disease is based on clinical fundus exam findings, family history, electrophysiologic testing, and genetic analysis. Electrooculogram (EOG) is a key factor in diagnosis and will be abnormal even when clinical exam findings are minimal. The EOG light-peak to dark-trough amplitude ratio is rarely higher than 1.4 (normal $\geq$ 1.8). The degree of EOG impairment does not correlate with visual acuity loss. Full-field electroretinogram (ERG) in is normal. Carriers of the VMD2 mutation who may not show any fundus changes will still have a definite subnormal EOG.

Genetic testing for mutations of the gene, VMD2, for Best disease is available.

Differential Diagnosis

Adult-onset vitelliform foveomacular dystrophy (pattern dystrophy)

Vitelliform lesions associated with basal laminar drusen or dominant drusen

Fundus flavimaculatus (Stargardt's disease) with large central flecks

Central serous chorioretinopathy

Serous detachments of the RPE

Toxoplasmic retinochoroiditis

Old foveal hemorrhages

Scars associated with macular degeneration or other causes of choroidal neovascularization

Prophylaxis

Potential carriers of Best disease can be screened by EOG or genetic testing. Prenatal diagnosis is possible once the familial mutation is identified.

Therapy

No therapy exists to treat or prevent Best disease.

Prognosis

Visual prognosis is generally good. Most patients retain reading vision in at least one eye. Severe visual loss is possible, however, if extensive macular atrophy or scarring occurs.

Epidemiology

Best disease is an autosomal dominantly transmitted disease of variable penetrance and expression.

Males and females are equally affected. Affected individuals or carriers will demonstrate an abnormal EOG.

Cross-References

- ▶ Electrooculogram
- ▶ Retina, Structure of

Further Reading

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Best Spherical Lens

- ▶ Spherical Equivalent

Best Vitelliform Macular Dystrophy

- ▶ Best Disease

Best-Fit Sphere

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Definition

The characterization of the corneal anterior or posterior surface elevation maps can be used. Elevation maps show the deviation of the elevation from a reference plane. This reference plane usually is a sphere, as a flat reference plane would not allow for local analysis of elevation irregularities. The BFS is calculated by the method of the least root mean square of deviation offer the area analyzed. Today different reference planes are being used for elevation maps, i.e., best-fit ellipsoids or best-fit spheres ignoring the central part of the cornea to detect early keratoconus.

Cross-References

- ▶ Keratoconus
- ▶ Topography (Corneal)

β, β-Carotene-4

- ▶ Canthaxanthin, Retinopathy

β-Hexosaminidase A Deficiency

- ▶ Tay-Sachs Disease (GM2 Gangliosidosis Type I)

Beta Carotene, Use and Dosage of

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Synonyms

Carotenoid; Vitamin A

Definition

Beta carotene is a type of carotenoid, a highly pigmented, fat-soluble compound found in a variety of green and yellow fruits and vegetables.

Absorbed in the small intestine, beta carotene is a provitamin that is converted to vitamin A. Vitamin A is an essential vitamin found in many tissues of the body, including the eye where it plays an important role in the visual transduction cycle. Vitamin A is transported to the eye as a vitamin A alcohol, or retinol. Retinol is stored in the retinal pigment epithelium (RPE). The aldehyde derivative of vitamin A, retinal, combines with the protein opsin in the photoreceptor outer segments of the retina to form the light-sensitive rhodopsin, an important visual pigment of the rod photoreceptors. Deficiency of vitamin A can result in visual symptoms and ultimately blindness. Toxicity is also possible with megadoses of vitamin A.

Indication

Vitamin A is essential for vision. Deficiencies can result from malnutrition, extreme diets, and poor intestinal absorption due to bowel abnormalities such as Crohn's disease and short bowel syndrome and from liver dysfunction seen with liver failure or alcoholism. Vitamin A deficiency results in nyctalopia and xerophthalmia with findings in the conjunctiva, cornea, and retina. Unfortunately, xerophthalmia is a major cause of blindness in children worldwide.

High doses of beta carotene and vitamin A may be helpful for some ocular diseases and disorders. The Age-Related Eye Disease Study (AREDS), a large, multicentered trial looking at high doses of antioxidants including beta carotene in patients with age-related macular degeneration (AMD), found that subsets of patients with AMD had reduced risk of progressing to severe forms of AMD with high-dose antioxidant supplementation. Patients with other retinal diseases such as advanced retinitis pigmentosa, Sorsby's fundus dystrophy, and Stargardt's disease may also benefit from beta carotene or vitamin A supplementation.

Contraindication

Use of beta carotene or vitamin A supplementation is not recommended for people who smoke or have a long-term history of smoking or who have known exposure to asbestos because of a potential increased risk of developing lung cancer.

People who are pregnant or may become pregnant should not take vitamin A supplementation because of the risk of major birth defects.

Use and Dosage

Dosage of beta carotene and vitamin A varies depending on use.

For patients with vitamin A deficiency and xerophthalmia over 1 year of age and not pregnant, a dose of 200,000 IU of vitamin A should be given immediately, the next day, and 2 weeks later.

For patients with less severe vitamin A deficiency, who have liver or kidney problems, and who are pregnant or are on dialysis, a doctor should be consulted for correct dosage.

For patients with macular degeneration, AREDS-based vitamins contain 15 mg of beta carotene (equivalent to 25,000 IU of vitamin A) in a daily dose.

Adverse Reactions

Excessive dosages of vitamin A, especially in children, can produce toxicity. Toxic changes can include exfoliation of the skin, alopecia, rash, hepatomegaly, splenomegaly, arthritic pains, hypothrombinemia, and increased intracranial pressure with papilledema. Use of isotretinoin (Accutane, Hoffmann-La Roche, Inc., Nutley, NJ), an oral form of vitamin A used to treat acne, has led to ocular adverse effects of anterior segment inflammation, keratitis sicca, contact lens intolerance, refractive changes, photophobia, and nyctalopia.

Interactions

Interactions with various medications and vitamin A have been reported. If other prescription drugs are being taken, a doctor should be consulted before high-dose vitamin A supplementation.

Cross-References

- ▶ Age-Related Macular Degeneration
- ▶ Antioxidants
- ▶ Carotenoids (Xanthophylls)
- ▶ Nyctalopia: Night Blindness
- ▶ Retina, Structure of
- ▶ Xerophthalmia

Further Reading

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Bevacizumab

- ▶ Antivascular Endothelial Growth Factor

Biber-Haab-Dimmer

- ▶ Corneal Dystrophies

Biber-Haab-Dimmer Dystrophy

- ▶ Lattice Dystrophy

Bicanalicular Intubation

- ▶ Silicone Intubation

Bichrome (Red-Green/Duochrome) Test

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Synonyms

Red-green/duochrome

Definition

Method of subjective refraction, based on chromatic aberration of the eye. A transparent eye chart is half coated with red and green filter. The density of the filters is chosen that the brightness for the eye based on wavelength 550 nm is equal. It is also equal for the dioptric difference caused by the chromatic aberration. Both halves of the chart have similar number and kind of optotypes, which can be graduated in visual acuity steps. Indication of the kind of ametropia is given through the comparison of clarity of the presented optotypes. Is the brightness dominant on the red half the eye is myopic an should be corrected with minus-lenses. Is it dominant on the green half the eye is hyperopic an should be corrected with plus-lenses. It can be used for validation of the correcting lens in far and near visibility.

Bietti Corneal Degeneration

- ▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
- ▶ Keratinoid (Spheroidal) Degeneration
- ▶ Spheroidal Degeneration

Bietti Crystalline Corneoretinal Dystrophy

- ▶ Bietti Crystalline Retinopathy

Bietti Crystalline Dystrophy

► Bietti Crystalline Retinopathy

Bietti Crystalline Retinopathy

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Synonyms

Bietti crystalline corneoretinal dystrophy; Bietti crystalline dystrophy; BCD

Definition

Bietti crystalline dystrophy is an autosomal recessive disease characterized by glistening crystalline-like changes in the posterior pole of the retina and atrophy of the retinal pigment epithelium (RPE) and choroid. Furthermore one-third of patients may present with crystal deposits in the superficial stromal layer of the paralimbal region of the cornea. This disease is named after Dr. G. B. Bietti, an Italian ophthalmologist, who described three patients with similar symptoms in 1937 (Okialda et al. 1993–2014; Ryan et al. 2012).

Epidemiology

Bietti crystalline dystrophy is rare and has been estimated to occur in 1 in 67,000 people (Okialda et al. 1993–2014). It is more common in people of East Asian descent, especially those of Chinese and Japanese background. Researchers suggest that Bietti crystalline dystrophy may be under diagnosed because its symptoms are similar to those of other eye disorders that progressively damage the retina.

BCD has also been reported in persons of Lebanese and Mexican origin and in persons of European origin presenting with retinitis pigmentosa (Okialda et al. 1993–2014; Ryan et al. 2012; Schubert 2014–2015).

Etiology

Bietti crystalline dystrophy is an autosomal disease caused by mutations in the *CYP4V2* gene, which was identified in 2004 by Gekka and colleagues. This gene is responsible of enzyme formation from the cytochrome P450 family of enzymes. The CYP4V2 enzyme is involved in a multistep process called fatty acid oxidation in which lipids are broken down and converted into energy. *CYP4V2* gene mutations that cause Bietti crystalline dystrophy impair or eliminate the function of this enzyme and are believed to affect lipid breakdown. However, it is unknown how they lead to the specific signs and symptoms of Bietti crystalline dystrophy (Okialda et al. 1993–2014).

Clinical Presentation

BCD is characterized by progressive atrophy and degeneration of the retinal pigment epithelium (RPE) and choriocapillaris, presenting with symptoms which overlap with other forms of retinal degeneration namely:

1. Reduced visual acuity – visual acuity can range from normal to hand motion (HM). Although the reduction in visual acuity has been reported to typically result in legal blindness by the fifth or sixth decade, central vision can sometimes be spared even in persons with severe disease.
2. Nyctalopia – progressive night blindness which is typical to many forms of retinal dystrophies.
3. Visual field loss – visual field defects correspond to areas of RPE and choriocapillaris

atrophy, manifesting as paracentral scotomas or peripheral field loss depending on the severity of the disease (Okialda et al. 1993–2014; Ryan et al. 2012; Schubert 2014–2015).

Onset of disease is typically during the second to third decade of life but ranges from the early teenage years to beyond the third decade. Marked asymmetry between eyes with respect to fundus appearance, reduction in visual acuity, and visual field loss is not uncommon.

Clinical Findings

Crystalline deposits in the corneal limbus can be found among approximately one-third of patients. It has been shown by several researches that these corneal deposits may be more common in patients of northern European descent than in Asians.

Funduscopic findings include small, glistening yellow-white crystal deposits scattered throughout the posterior pole, which sometimes might extend to the mid-periphery. Both diffuse and localized forms of retinal degenerative changes may be found. It has been described that the crystalline deposits tend to diminish or even disappear in areas of severe chorioretinal atrophy as the disease progresses in severity (Okialda et al. 1993–2014; Ryan et al. 2012). Areas in which crystals are still present may represent the retina that is still only mildly degenerated or in the progress of degenerating. The retinal vessels and optic nerve are usually normal but there may be some vascular attenuation and/or disc pallor in advanced cases.

Complications may include development of macular hole and choroidal neovascularization (CNV) in rare cases.

Furthermore the cholesterol or cholesterol esters can be found in fibroblasts as well as circulating lymphocytes, suggesting that the disorder may be a systemic abnormality of lipid metabolism.

Further Tests

Fluorescein angiography (FA) shows patchy hypofluorescent areas of RPE and choriocapillaris atrophy and a generalized disturbance of the RPE.

Electroretinogram (ERG) can show varying degrees of rod and cone dysfunction, ranging from normal to reduced amplitudes of scotopic and photopic responses to undetectable responses. ERG amplitude reduction often parallels the degree of fundus pigmentary changes.

Spectral domain optical coherence tomography (SD-OCT) is an important tool for diagnosis and management of BCD. The degeneration in BCD detected by OCT is most prominent in the outer retina layers. It is characterized by findings of hyper-reflective dots which represent the crystalline deposits that reside in the RPE-choriocapillaris complex. In addition to these crystalline deposits, other abnormalities due to loss of retinal tissue such as retinal tubulation can be found (Okialda et al. 1993–2014; Ryan et al. 2012).

Diagnosis

The majority of cases are diagnosed by the clinical appearance and can be confirmed by molecular testing of *CYP4V2*. Furthermore, testing for at-risk relatives who may be carriers and prenatal testing in high-risk pregnancies are possible (Okialda et al. 1993–2014).

Differential Diagnosis

Crystalline deposits in the retina may be associated with:

- Primary hyperoxaluria type 1 and primary hyperoxaluria type 2
- Cystinosis
- Sjögren-Larsson syndrome

- Drug toxicity (e.g., the tamoxifen, the anesthetic methoxyflurane, the oral tanning agent canthaxanthin)
- Drug abuse (talc retinopathy)
- Idiopathic juxtafoveal retinal telangiectasia

Obtaining detailed medical history, thorough systemic and ocular examination, and fluorescein angiography are usually sufficient to exclude these conditions (Okialda et al. 1993–2014; Schubert 2014–2015).

Therapy

No treatment for BCD currently exists. Patients may benefit from low vision aids. In the future, findings from gene research might be helpful in finding treatments for patients with BCD (Okialda et al. 1993–2014).

Though CNV is uncommon in BCD, anti-vascular endothelial growth factor (anti-VEGF) therapy can be used to treat this complication.

Prognosis

The presenting symptom, rate of disease progression, and disease severity are also highly variable in BCD, even among those of the same age, within the same family, and with the same *CYP4V2* mutation. However, with time, loss of peripheral visual field, central acuity, or both result in legal blindness in most affected individuals (Okialda et al. 1993–2014).

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Bietti's Corneoretinal Crystalline Dystrophy

▶ Corneoretinal Dystrophy, Bietti's Crystalline

B

Bietti's Crystalline Dystrophy

▶ Corneoretinal Dystrophy, Bietti's Crystalline

Bietti's Tapetoretinal Degeneration with Marginal Corneal Dystrophy

▶ Corneoretinal Dystrophy, Bietti's Crystalline

Bifocal Intraocular Lens

▶ Apodized Diffractive Intraocular Lens

Bifocal Lenses

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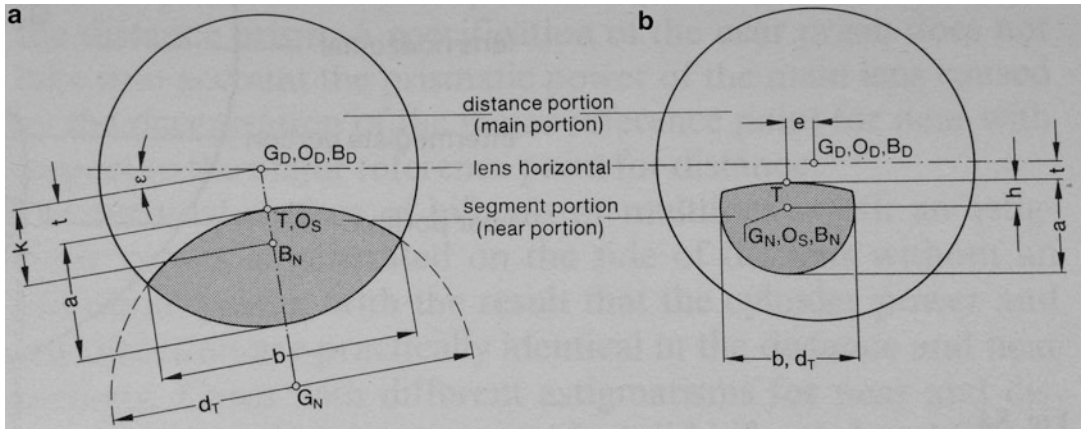
Synonyms

Multifocal lenses

Definition

Bifocal and multifocal lenses have different, visibly separate areas characterized by their different spherical powers. A bifocal lens is composed of a



Bifocal Lenses, Fig. 1 (**a**) Rotatable (**b**) nonrotatable

main lens and additional or segment lens. A trifocal has two segment lenses which are either separated or adjacent. The area in which the power of the main lens alone is effective is called the main portion. Here the lens has the same dioptric power as an equivalent single-vision lens. The area in which the powers of the main lens and the additional lens are combined is called the additional or segment portion. The dioptric power of the segment portion must not be confused with the power of the segment lens in its own right.

In the majority of bifocal and multifocal lenses, the optical center of the segment lens is decentered with respect to the optical center of the main lens.

The main portion or a segment portion can be used for distance vision (distance portion), intermediate vision (intermediate portion), or near vision (near portion). In most cases, the main portion is the distance portion. A dividing line separates the different portions (Fig. 1).

The segment lenses are either cemented, fused – in which case they have a different refractive index – or ground onto the surface of the main lens. While the main portion is generally point focal, this is not always the case in the segment portion. If the segment portion is fused onto the main portion, it is more favorable for point-focal imagery to perform the fusion on the back surface of the lens.

Different shapes are possible for the segment portion, a distinction being made between rotatable and nonrotatable types. Circular or types located at the periphery of the main lens are rotatable.

Prismatic Jump

If different prismatic powers exist on either side of the dividing line between two portions of a bifocal lens, the object perceived appears to jump when the fixation line of the eye crosses the dividing line. The difference between these two prismatic powers is called the prismatic or image jump, as it is not the object but the image produced by the spectacle lens which is in fact jumping.

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Bilobed Flap

▶ Transposition Flaps, for Lateral Canthal Defects

Binocular Diplopia

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Definition

Diplopia is the term used to describe double vision or the perception of two images of a single object. Diplopia can be classified as either monocular or binocular. Binocular diplopia refers to double vision that is present with both eyes open, but which resolves when either eye is closed. In contrast, monocular diplopia persists in the affected eye(s) even when the other eye is closed and can be unilateral or bilateral (Guluma 2014). Binocular diplopia is the physiologically appropriate response when an object falls onto two different areas of the intact retina, the fovea of one eye and the non-foveal region of the other eye. This then causes the perception that a single object has two different locations in space. The most common cause of binocular diplopia is misalignment of the visual axes (Buffenn 2008). On physical exam, the patient will often have ocular deviation of one of their eyes (Perlmutter and Moster 2014). Presentation of binocular diplopia will vary with age since young children are better able to ignore the problem than older children and adults (Buffenn 2008). Also, many patients will describe the change in vision as being "blurry" rather than have frank double vision. When assessing a patient, it is important to note that ocular movement in which direction(s) causes the double vision occur and whether it is worse when focusing at objects at a distance or upclose, as this helps guide the diagnosis (Guluma 2014).

Treatment for binocular diplopia requires identification and appropriate therapy for the underlying etiology.

Prognosis is dependent upon the underlying etiology.

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Binocular Indirect Ophthalmoscope (BIO), in Retinal Examination

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Synonyms

BIO

Definition

Precise binocular viewing of the fundus with adjustments from 48 to 75 mm in order to examine patients with pupils less than 2 mm in size.

Basic Characteristics

There are numerous advantages to using the indirect ophthalmoscope. The image is not affected by the patients' refractive power. For children, this technique is easier to use. It is also used in operating room for cryo-/scleral buckling. With superior illumination, full visualization of periphery is achieved. Disadvantages to this technique include difficulty to master, reversed and inverted image, and relative lack of magnifications (Figs. 1 and 2).

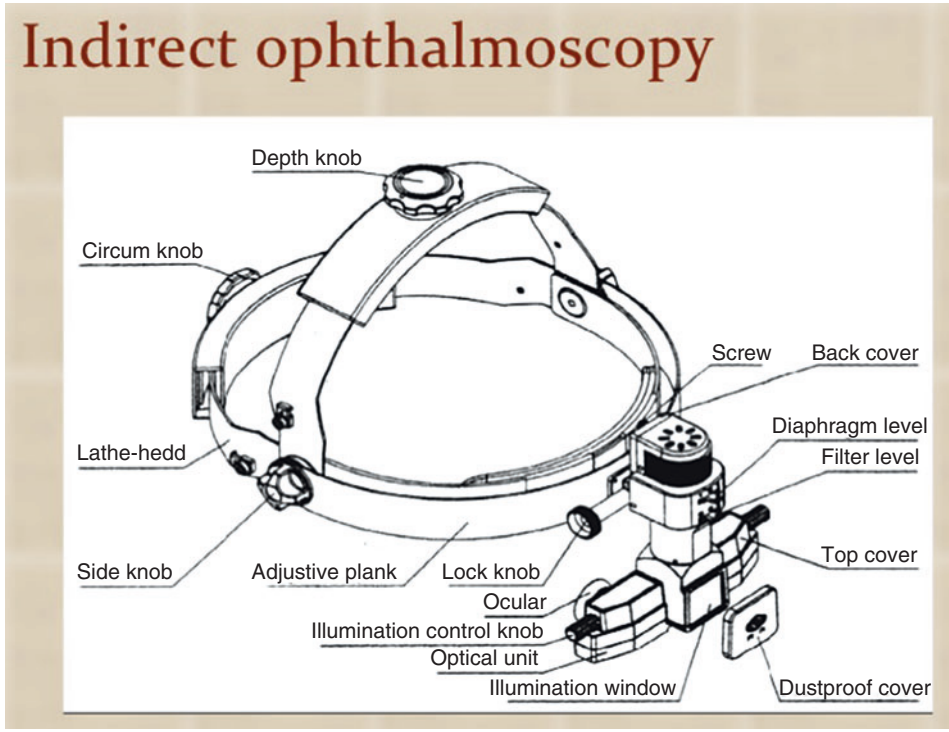
Comparison with Direct

Feature	Direct	Indirect (+20lens)
Magnification	14×	3×
Field diameter	2DD	9DD
Ratio of area	1	20
Illumination	Limited	High
Depth of focus	Small	Large
Stereopsis	Absent	Present
Orientation of image	Direct	Inverted, reversed
View of periphery	Limited	Full
Scleral indentation	Difficult	Easy

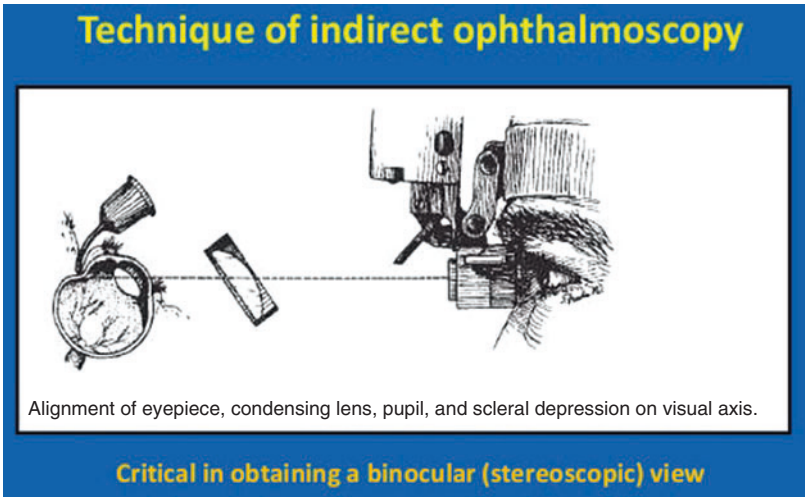
Examination Technique

The headband piece is adjusted to be sitting in a stable position. Halogen illumination is turned on. If examining the periphery, the diffuser filter is turned on. There is a convergence control for very small pupils.

The patient is either sitting in a reclined chair or lying on a couch. The pupil may be dilated and the



Binocular Indirect Ophthalmoscope (BIO), in Retinal Examination, Fig. 1 Indirect ophthalmoscopy



Binocular Indirect Ophthalmoscope (BIO), in Retinal Examination, Fig. 2 Technique of indirect ophthalmoscopy

room dimmed. Alignment of the patients' eye and the examiner's eye is in a straight line. Check for the red reflex, then bring the condensing lens in front of the patient's eye. Some units come with an advanced video alignment system to have precise orientation for accurate viewing. The image is inverted and reversed. The ora serrata can be viewed by scleral indentation with the free hand of the examiner using local anesthetic like proparacaine, tetracaine, or proxymetacaine.

BIO

▶ Binocular Indirect Ophthalmoscope (BIO), in Retinal Examination

Biometry, Use and Principle of

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Definition

Axial measurement of the eye by ultrasound.

Purpose

Biometry of the eye prior to cataract or refractive surgery.

Principle

Ultrasonic biometry is based upon the differential return of ultrasonic waves by varying tissue types in the eye. Sound waves are emitted by a piezoelectric crystal and delivered with a probe. For axial measurements, the probe is placed perpendicular to the corneoscleral surface. Ultrasonic biometry can either be performed with the contact method when direct contact between the corneal surface and probe is made or with immersion biometry applying an eyecup between the eyelids filled with immersion fluid (e.g., balanced salt solution, methylcellulose). Optical biometry is based on partial coherence interferometry, Scheimpflug imaging, or optical coherence tomography.

Indication

Biometry is applied for measurement of central corneal thickness, anterior chamber depth, lens thickness, and axial length of the eye.

Advantage/Disadvantage

Ultrasonic biometry is a reliable method for biometry of the eye prior to cataract or refractive surgery. A correct position of the probe is mandatory during measurement and the results depend on the experience of the examiner. In contrast to optical biometry, ultrasound biometry can be performed even with opaque optical media such as dense cataract or vitreous hemorrhage. Compared with optical biometry ultrasound biometry is more time consuming and requires topical anaesthesia of the eye.

Cross-References

- ▶ Optical Coherence Tomography
- ▶ Partial Coherence Interferometry

Further Reading

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Biomicroscopy, Ultrasound

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Synonyms

UBM

Definition

Ocular imaging applying ultrasound with frequencies of 35 MHz and above.

Purpose

Ultrasound biomicroscopy allows noninvasive real-time imaging of anatomy and pathology of the anterior segment of the eye.

Principle

Ultrasound consists of waves of compression and rarefaction propagating through a medium. Acoustic reflection occurs at interfaces between regions of different acoustic impedance. Scattering occurs where these discontinuities are smaller than a wavelength. Attenuation of ultrasound occurs as it propagates through tissues as a consequence of reflection, scattering, and absorption.

Indication

Ultrasound biomicroscopy is applied for imaging of the cornea, iridocorneal angle, anterior chamber, iris, ciliary body, and the lens. Ultrasound biomicroscopy can be used for diagnostics in anterior segment neoplasms, trauma, and glaucoma.

Contraindication

In open-globe injury, ultrasound biomicroscopy should only be done when the potential benefit justifies the potential risk.

Advantage/Disadvantage

In contrast to optical anterior segment imaging technologies (optical coherence tomography, Scheimpflug imaging, scanning slit-lamp systems), ultrasound biomicroscopy can be applied to visualize structures of the anterior segment obscured by the iris and the sclera and with opaque media. Ultrasound biomicroscopy is

more difficult to use than optical imaging technologies and needs fluid coupling to the eye.

Cross-References

- ▶ Anterior Segment
- ▶ Optical Coherence Tomography
- ▶ Scheimpflug Imaging

Further Reading

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Biomicroscopy, Ultrasound, of Anterior Segment

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Synonyms

High-resolution ultrasound biomicroscopy, UBM

Definition

UBM is a type of ultrasonography which uses a high-frequency transducer (35–50 M Hz, compared to standard ultrasonography which uses a 10 M Hz transducer), which allows higher resolution of structures, but shallower penetration of tissue, and produces excellent imaging of the anterior segment. This technique produces resolution of about 20–50 μm; however, tissue penetration is limited to approximately 5 mm.

Purpose

To visualize anatomy of the anterior segment including the anterior chamber angle

B

Principle

The higher the frequency emitted by the transducer, the higher the resolution of the tissue structures that can be obtained. However, the higher the frequency emitted by the transducer, the shallower the tissue penetration, and therefore deeper structures are not visualized. With lower-frequency transducers, as in conventional ultrasound, deeper structures can be visualized but with much less resolution.

Indication

UBM is used to visualize details of the cornea, drainage angle, ciliary body, supraciliary space, zonules, and iris and to characterize the relationship of these structures to each other. It is helpful in patients with plateau iris and has been used to show reversal of iris concavity after laser peripheral iridotomy in patients with pigmentary glaucoma. It can help identify angle recession and malignant glaucoma.

Contraindication

Corneal abrasion, keratitis, infection, hyphema, acute trauma, penetrating injury, or perforated globe.

Advantage

Noninvasive, relatively inexpensive.

Disadvantage

Limitation to the depth of structures which can be visualized, requires supine positioning and much cooperation from the patient.

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Biopsy

- ▶ Excisional Biopsy
- ▶ Full-Thickness Eyelid Biopsy
- ▶ Incisional Biopsy

Bipolar Cells

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Definition

Excitatory inner retinal neurons that convey gradients between photoreceptors and retinal ganglion cells. Release of a single neurotransmitter (glutamate) by the cone photoreceptors causes OFF bipolar cells to depolarize and ON bipolar cells to hyperpolarize. ON bipolar cells utilize a metabotropic glutamate receptor and have a sign-inverting synapse with the cone, while OFF bipolar cells utilize an ionotropic glutamate receptors and have a sign-conserving synapse with the cone. Rod photoreceptors connect to a single, structurally distinct, bipolar cell – the rod bipolar cell.

Cross-References

- ▶ Arachnoid Mater, Optic Nerve
- ▶ Color Vision, Three Cone Opsins
- ▶ Electrical Response of the Retina to a Light Stimulus, The
- ▶ Electroretinogram
- ▶ Light Adaptation
- ▶ Retina, Structure of

Birdshot Retinochoroidopathy (Vitiliginous Chorioretinitis)

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Synonyms

Vitiliginous chorioretinitis (no longer used)

Definition

Birdshot retinochoroidopathy (BSRC) is a rare distinct intraocular inflammatory condition. It is characterized by the presence of multiple cream-colored round or oval choroidal lesions in the post-equatorial region, mainly the peripapillary area at the level of the outer retina/choroid. The lesions appear in a pattern resembling the scatter of birdshot pellets from a shotgun (Nussenblatt et al. 1982; Priem et al. 1988).

Pathogenesis

BSRC is considered a T-cell-mediated disease. Findings of higher than normal levels of IL-17 in the serum and aqueous humor of affected patients suggest that the Th17 subset is involved in the pathogenesis of BSRC (Miossec et al. 2009; Brezin et al. 2011). About 95% of patients with BSRC are positive for HLA A-29 – the highest class 1 haplotype association of any disease – but its pathogenic role remains unclear. Molecular mimicry triggered by antecedent infection is a popular hypothesis.

Epidemiology

BSRC typically occurs in the sixth decade of life. It has a slight gender predilection for women and a

higher incidence in white individuals of Northern European descent (Nussenblatt et al. 1982; Priem et al. 1988). There is no published data on the incidence and prevalence of this disorder. Small retrospective case series reported a 0.6–1.5% rate of diagnosing birdshot chorioretinopathy among patients who were referred to tertiary care centers for uveitis, accounting for 6–7.9% of all posterior uveitides.

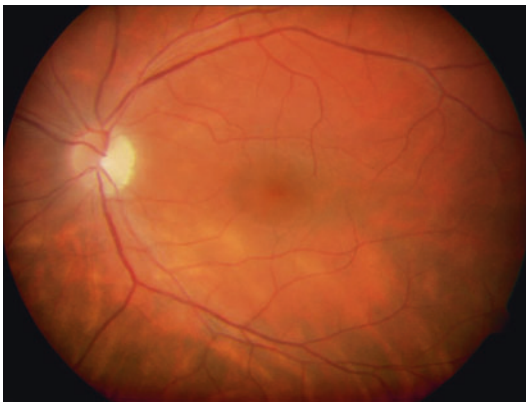
Clinical Presentation

Patients usually complain of a gradual decrease in visual acuity, floaters, photopsia, and nyctalopia, and impaired color vision, with symptoms surpassing clinical findings. The disturbances may be initially asymmetric, evolving to bilateral disease. A high index of suspicion is required in the early stages.

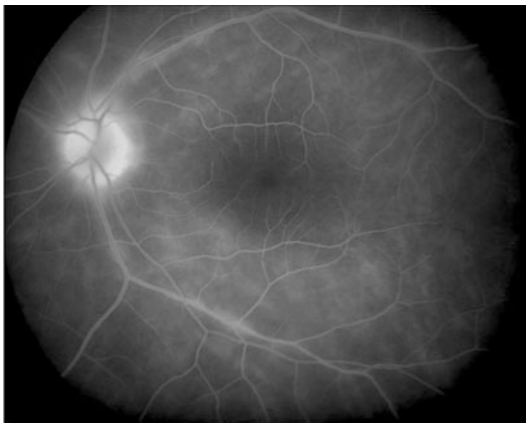
Diagnosis

The diagnosis of BSRC is based on clinical findings of at least three typical "birdshot" lesions. The appearance of the lesions may be preceded or accompanied by mild inflammation, without anterior segment complications.

Multimodal imaging of the retina and choroid provides structural and functional information and is important to establish the diagnosis. Figure 1 is a color fundus photograph of representative chorioretinal lesions. Fluorescein angiography (Fig. 2) demonstrates retinal vascular leakage, with no apparent involvement of the overlying retina or underlying retinal pigment epithelium (RPE). Indocyanine green angiography (ICGA) (Fig. 3), seldom used nowadays for other indications, shows the typical pattern of oval hypofluorescent lesions, located mostly along the medium-sized choroidal vessels. In the early stages of disease, some lesions may represent hypoperfusion of small choroidal vessels, whereas others represent inflammation, producing a masking effect. In long-standing disease, the choroidal vessels appear well-preserved, and retinal involvement becomes

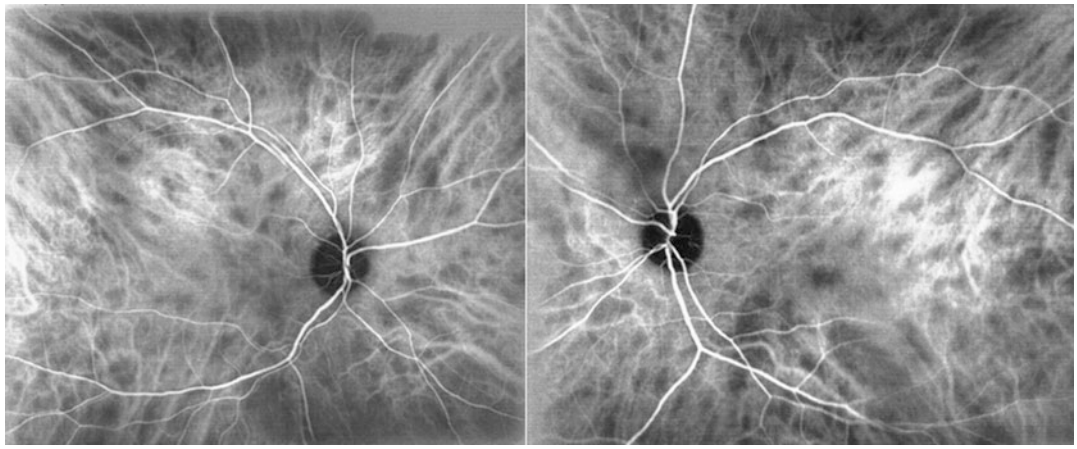


Birdshot Retinochoroidopathy (Vitiliginous Chorioretinitis), Fig. 1 Color photograph of the left eye of a 43 year-old male demonstrating typically scattered oval creamy subretinal lesions



Birdshot Retinochoroidopathy (Vitiliginous Chorioretinitis), Fig. 2 Flurescein angiography of the same eye in Fig. 1, demonstrating mild retinal vascular leakage, optic nerve head leakage and faint appearance of the subretinal lesions

clinically evident. The hypofluorescent spots are thought to represent foci of choroidal atrophy or persistent choroidal granulomas. Fundus autofluorescence has gained popularity in the recent years owing to the high-quality images provided by confocal imaging techniques, mainly of the RPE-outer retina complex. The hypoautofluorescent areas correlate with RPE atrophy but not necessarily with visible fundus lesions, suggesting both choroidal and RPE damage in BSRC. Macular hypoautofluorescence indicates



Birdshot Retinochoroidopathy (Vitiliginous Chorioretinitis), Fig. 3 Indocyanine green angiography of both eyes of the same patient, demonstrating the typical oval hypofluorescent spots, located mostly along medium-sized choroidal vessels

macular RPE damage and correlates with poor visual outcome (Koizumi et al. 2008).

Abnormalities on electroretinography (ERG) are often found in patients with BSRC, reflecting retinal dysfunction. An impaired pattern ERG in the early stages indicates macular edema. Photopic and scotopic ERG findings support the concept that the neuro-retinal dysfunction is primarily located in the inner retina, and this is manifested by a low b:a wave ratio.

Though not essential for diagnosis, positive findings of HLA-29 may serve as supportive evidence (Levinson et al. 2006). HLA A-29 is an inefficient screening factor for BSRC because it is present in about 8% of the general population.

Differential Diagnosis

Posterior uveitis entities with similar deep retinal and subretinal lesion should be excluded. These include infectious diseases, such as syphilis and tuberculosis, and noninfectious diseases, i.e., sarcoidosis and masquerade syndrome. Patients who present initially with retinal vascular leakage, while retino-choroidal lesions are faint, will undergo workup for retinal vasculitis. In typical cases, no such workup is required.

Clinical Course

BSRC has a chronic clinical course, with slow deterioration of visual functions including visual acuity and visual fields, and a steady increase in structural damage to the retina. Cystoid macular edema (CME), which occurs in up to 50% of patients, is the most common cause of central visual impairment. Later in the disease course, macular thinning and atrophy may evolve. Photoreceptor dysfunction also occurs later. The progressive retinal involvement with diffuse atrophy affecting mainly the outer layers resembles the behavior of a neurodegenerative disorder (Fardeau et al. 1999; Herbort et al. 2004).

Treatment

The mainstay of treatment of BSRC is corticosteroids followed by chronic immunosuppression. The immunosuppressive drugs are

administered mainly because of the unacceptable side effect profile of long-term corticosteroids in the required dose. They usually include antimetabolites, such as methotrexate, azathioprine, and mycophenolate mofetil. Cyclosporine may also be a favorable option owing to the presumed T-cell involvement in the pathogenesis of the disease, but it is less likely to be used in elderly patients because the risks of renal toxicity and hypertension. Biologic antitumor necrosis alpha (TNF-α) agents have also shown a beneficial effect, specifically in refractory cases (Artornsombudh et al. 2013).

Since BSRC is limited to the ocular area, local treatment is appealing, but the modalities need to be long-acting. Intravitreal Retisert (fluocinolone acetonide) implants have been suggested, but they require surgery for both implantation and explantation and are associated with a need for cataract surgery within 3 years in all patients and trabeculectomy surgery in 40% of patients. Ozurdex, an injectable implant, may also be beneficial, but its therapeutic effect usually lasts only 4–6 months, and repeated injections are necessary (Lowder et al. 2011). A study of posterior uveitis, the Multicenter Uveitis Steroid Treatment Trial, reported similar efficacy for systemic and local therapy, with acceptable side effects of systemic intramuscular therapy (The Multicenter Uveitis Steroid Treatment (MUST) Trial Research Group et al. 2011).

However, the effect of treatment on the clinical course of BRSC is still equivocal. One study suggested that treatment did not affect visual outcome, with visual deterioration occurring at a similar rate with and without treatment (Rothova et al. 2004). By contrast, one case report demonstrated restoration of the retinal structure accompanied by visual field improvement following immunosuppressive therapy (Forooghian et al. 2010). A recent longitudinal study showed that chronic progression occurred despite treatment, although in patients receiving long-term immunosuppression (with mycophenolate mofetil in this study), the visual fields were preserved, implying a beneficial effect on peripheral retinal function (Tomkins-Netzer et al. 2014).

The choice of the best targeted therapy still needs to be investigated in controlled clinical trials.

Follow-Up

Long-term monitoring is required. Visual acuity and visual fields should be assessed regularly. It is noteworthy that visual acuity may be preserved and clinical signs and symptoms may improve despite retinal function deterioration. Therefore, clinical symptoms cannot serve as reliable indicators of disease progression, complicating clinical decision making. The pattern of photoreceptor dysfunction – initially rods followed by cones – reflects the late preserved visual acuity. Optical coherence tomography (OCT) is used regularly to document and follow CME. ERG has also become an important objective tool for monitoring disease activity and response to treatment. Impaired pattern ERG usually reflects macular edema at early stages of the disease, and improvement correlates with resolution of the edema. Delayed 30 Hz cone flicker implicit time, often present before treatment, appears to be a sensitive indicator of retinal function (Holder et al. 2005).

Summary

BSCR is a rare chronic disease causing diffuse atrophic damage; therefore, visual function should be assessed based on VA, VF, and electrophysiology of the retina.

Early treatment with immunosuppression is correlated with better visual outcome. Biologic agents may offer benefit in refractory cases. Local intravitreal modalities may be used in selected cases.

Long-term monitoring is required. The choice of the best targeted therapy should be studies in controlled clinical trials.

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Bitemporal Hemianopsia

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Definition

Bitemporal hemianopsia (BTH) is a form of visual field loss of the temporal half of the visual field in both eyes that generally respects the vertical midline. This type of vision loss results from disruption of the nasal crossing fibers of both eyes due to lesions at the optic chiasm. Bilateral retinal lesions in the nasal portion of the retina or tilted optic nerves may mimic a bitemporal hemianopsia from chiasmal lesions.

Etiology

A BTH is caused by a lesion at the optic chiasm. The most common chiasmal lesions in adults

include pituitary adenoma, craniopharyngioma, meningioma, or suprasellar internal carotid artery aneurysm. In children, optic pathway glioma and dysgerminoma are more common than meningioma or aneurysm, but pituitary adenoma and craniopharyngioma remain in the differential diagnosis. Pituitary lesions arise from the pituitary gland in the sella turcica and then extend to the suprasellar space and thus compress the nasal crossing fibers in the chiasm from below producing a BTH that is denser superiorly. In contrast, suprasellar lesions arising from above the optic chiasm may produce a BTH that is denser inferiorly. In addition to neoplastic etiologies, trauma (i.e., traumatic chiasmopathy), demyelination (e.g., multiple sclerosis, neuromyelitis optica), and infiltrative and inflammatory (e.g., sarcoidosis) or toxic/nutritional (uncommon) chiasmal lesions may also produce a BTH.

Diagnosis

A cranial magnetic resonance imaging (MRI) with and without contrast is usually indicated for patients with an unexplained BTH. MR or computed tomography (CT) angiography can be used to identify suprasellar aneurysms if suspected clinically.

Differential Diagnosis

The differential diagnosis includes the neoplastic (most common) and less commonly vascular, demyelinating, and inflammatory diseases (e.g., sarcoidosis, lupus, and lymphocytic hypophysitis).

Clinical

Patients with BTH, depending on etiology, may also present with other symptoms and signs (e.g., headaches) or endocrine abnormalities in pituitary lesions (e.g., acromegaly, Cushing syndrome, pituitary apoplexy, hypopituitarism, central diabetes insipidus, and hyperprolactinemia). Patients may also experience non-paretic diplopia (double vision) in the absence of extra-ocular muscle palsies (i.e., non-paretic diplopia). This is believed to be due to patients' inability to fuse the two nonoverlapping intact remaining nasal visual fields leading to slip of the images (i.e., the retinal hemifield slide phenomenon).

Treatment

Treatment of BTH depends on the etiology. Surgical treatment is generally recommended for symptomatic compressive BTH. Infectious etiologies are treated with antibiotics; and inflammatory or demyelinating etiologies are treated with immunosuppressive or immunomodulatory agents. Some pituitary adenomas which are prolactin secreting (i.e., prolactinomas) can be treated with bromocriptine or cabergoline (dopamine agonists that can suppress prolactin production) and can cause the tumor to shrink.

Prognosis

Recovery of vision depends on the extent of damage to the optic chiasm and the underlying etiology.

Epidemiology

There is no racial predilection for BTH, but the epidemiology of BTH depends upon etiology. For example, pituitary adenomas are quite common with a prevalence of about 16% in the general population.

Further Reading

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Bitoric

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Definition

Term of contact lens optics for rigid contact lenses with two toric surfaces. If corneal astigmatism is too high for correction with hard lenses or if internal astigmatism is higher than corneal astigmatism, it is indicated to use bitoric hard contact lenses. For the surface design of the lens, that means that both sides are toric.

Black Hidrocystoma

▶ Sweat Glands of Eyelid, Tumors Arising in

Blepharitis

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Definition

Blepharitis is an inflammation of the eyelid that causes symptoms of itching, tearing, redness, and swelling. It can occur on the anterior or posterior eyelid and may be caused by bacterial infection, seborrheic dermatitis, oil gland dysfunction, or other skin conditions like rosacea.

Cross-References

▶ Blepharoconjunctivitis
▶ Seborrheic Blepharitis

Blepharochalasis

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Definition

An eyelid disorder with episodes of painless edema that leads to atrophic changes in the eyelid skin.

Etiology

Numerous triggers have been reported including menstruation, fatigue, upper respiratory tract infections, bee stings, fever, wind, emotional stress, minor lid trauma, and lymphocytic leukemia, among others. Most often however, there is no known cause for blepharochalasis.

Clinical Presentation

Recurrent episodes of painless, non-erythematous edema of the upper eyelids. The edema typically does not resolve with steroids or antihistamines. In severe cases, the lower eyelids may be involved. Episodes typically last a few hours to days. Frequency of attacks varies from weekly to three to four times per year. The episodes typically decrease in severity over time and most cases become relatively quiescent. After numerous episodes the eyelid skin becomes wrinkled, lax, discolored, thinned, and invested with tortuous vessels. The skin has been described as “tissue paper”-like. Ptosis with good levator function is commonly coexistent. Lateral and medial canthal attachments to the eyelid skin tend to become lax with time as well. In certain variants orbital septal weakness develops and leads to marked prolapse of orbital fat. More atrophic variants tend to have eyelids with a hollow appearance.

Diagnostics

Clinical examination, biopsy.

Differential Diagnosis

Dermatochalasis, recurrent angioedema, hereditary angioedema, Melkersson-Rosenthal syndrome, cutis laxa.

Therapy: Treatment should be undertaken only in the quiescent phase of the disease. The primary treatment for blepharochalasis is surgical including blepharoplasty, recreation of the eyelid crease, resuspension of the lacrimal gland, removal of orbital fat, and levator aponeurosis repair. Special attention should be paid to patients undergoing ptosis repair with blepharochalasis syndrome as patients are frequently overcorrected. Lateral canthal tendon repair is often indicated and should precede ptosis repair to avoid temporal peaking of the eyelid. Medial canthal tendon placation may be indicated as well. Lower eyelid disease may be treated with blepharoplasty and/or canthoplasty. It is useful to take pathologic specimens for analysis during surgical repair.

Prognosis

Episodes tend to become less frequent with age. Recurrences may occur after surgery. The length of postoperative attacks does not seem to be influenced by corticosteroid use or cold compresses.

Epidemiology

As of 2007 only 67 cases had been reported in the literature – 22 men and 45 women. The average age of onset was 11 years old. Twenty-seven of 67 cases were unilateral.

Cross-References

- ▶ Edema, Eyelid
- ▶ Eyelid Erythema
- ▶ Infraciliary Blepharoplasty Incision, for Anterior Orbitotomy

Further Reading

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Blepharoconjunctivitis

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Synonyms

Blepharitis; Conjunctivitis; Eyelid inflammation

Definition

[The ubiquitous combination of eyelid and conjunctival inflammation caused by multiple etiologies including infection, inflammatory disease, and carcinoma.]

Cross-References

- ▶ Basal Cell Carcinoma of Eyelid
- ▶ Sebaceous Carcinoma/Adenocarcinoma
- ▶ Sebaceous Glands of Eyelid, Tumors Arising in

Blepharospasm

- ▶ Benign Essential Blepharospasm: Neuro-ophthalmic Considerations

Blindness of Dahalach, The

- ▶ Keratinoid (Spheroidal) Degeneration
- ▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
- ▶ Spheroidal Degeneration

Blizzard Keratopathy

- ▶ Hurricane (Vortex) Keratopathy

Bloch-Siemens Syndrome

▶ Bloch-Sulzberger Syndrome (Incontinentia Pigmenti)

Bloch-Sulzberger Disease

▶ Bloch-Sulzberger Syndrome (Incontinentia Pigmenti)

Bloch-Sulzberger Syndrome (Incontinentia Pigmenti)

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Synonyms

Bloch-Siemens syndrome; Bloch-Sulzberger disease; Incontinentia pigmenti (IP); Melanoblastosis cutis; Nevus pigmentosus systematicus

Definition

Bloch-Sulzberger syndrome is a rare disorder characterized by X-linked dominant inheritance and integumentary, central nervous system (CNS), and ocular manifestations. It was defined in the literature by Bruno Bloch in 1926 and Marion Sulzberger in 1928, both dermatologists. Abnormal skin pigmentation is observed in almost all patients affected, and lesions progress through four classic stages: blistering, verrucous, swirling macular hyperpigmentation, and linear hypopigmentation. Alopecia and dental irregularities are also seen. CNS pathology occurs less frequently and can take the form of cognitive delay, seizures, or spastic paralysis. The syndrome is typically observed in females, as the mutation is often lethal to males in utero.

Etiology

Roughly 80% of patients studied share a deletion in the *IKBKG* or *NEMO* gene on the long arm of the X chromosome (Xq28). Two intact copies of *NEMO* are required for effective counterbalance of proapoptotic signals. *NEMO* is key to the activation of nuclear factor kβ (NF-kβ), which in turn protects cells against the proapoptotic signal tumor necrosis factor α (TNF-α).

Clinical Presentation

Typically, the ocular manifestations of this syndrome are retinal. The damage manifests along a spectrum, ranging from normal vision to blindness in approximately 40% of patients. The mechanisms resemble those of retinopathy of prematurity. Retinal vaso-occlusion is an early finding, leading to patchy retinal infarction and subsequent neovascularization and chorioretinal scarring. Arteriovenous anastomoses form, marked by anomalous vessel morphology, and are coupled with avascular regions, usually at the periphery. This can progress to retinal detachment and resultant loss of vision, with poor response to surgical correction. Retinal detachments occur most commonly in the first year of life, and almost all occur within the first 2–3 years of life.

In addition, the vascularization of the normal foveal avascular zone in several patients has been found to contribute to decreased visual acuity. Hypoperfusion can affect the optic nerve as well,

producing optic nerve pallor. In a subset of patients, optic nerve atrophy also contributes to visual loss. Central nervous system involvement due to vascular occlusive disease can result in occipital lobe infarction, homonymous hemianopic visual field loss, and cortical blindness.

It has been postulated that the vaso-occlusion results from an eosinophilic vasculitis. Eosinophilic infiltrates have been described in the dermal vasculature, as well as in the brain and retina. The NF-kβ signaling pathway is thought to play a role in this, as it is involved in eosinophil chemotaxis via the intermediate signal eotaxin.

Other ocular changes occur less commonly and include scleral and conjunctival pigmentation, neovascularization-related vitreous hemorrhage, corneal and lens abnormalities, myopia, amblyopia, and strabismus.

Diagnosis

It is recommended that all patients with incontinentia pigmenti undergo full eye examinations and consideration for fluorescein angiography. Many authors recommend that patients should be screened at least once followed by monthly or annual screening varying by case and severity. Fluorescein angiogram is superior to indirect ophthalmoscopy in the identification of neovascularization and occlusion and allows pathology to be recognized and thus treated earlier in the course of the disease. In adults diagnosed with this syndrome, it is important to be cognizant of new-onset retinal detachment, particularly at the borders separating avascular and adequately perfused retina. Symptomatic patients should be examined carefully.

Differential Diagnosis

Naegeli syndrome, retinopathy of prematurity, and familial exudative vitreoretinopathy.

Therapy

The progression of vascular insults can be treated by application of laser photocoagulation or cryoablation to the ischemic segments of the retina. However in some cases the retina goes on to detach regardless.

Prognosis

Prognosis varies in accordance with severity of the disease in each patient. In the case of vision, prevention of further retinal detachment is occasionally possible with laser or cryoablation.

Epidemiology

Less than 1,200 cases of IP have been reported in the literature to date. The syndrome is most prevalent among Caucasians. It is possible that it is underdiagnosed, as the obvious skin findings can be mild in some patients.

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Blood-Aqueous Barrier

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Definition

The blood-aqueous barrier is located in the nonpigmented cells of the ciliary epithelium.

Structure

The ciliary epithelium consists of the pigmented layer which is located on the stromal side and the nonpigmented layer that faces the posterior chamber. The blood-aqueous barrier is located on the nonpigmented layer. These cells are connected by tight junctions of the leaky type. However, they do not form a solid barrier allowing some protein to pass from the ciliary processes into the posterior chamber.

The blood-retinal barrier and the blood-aqueous barrier appear to overlap in the pars plana.

Function

The blood-aqueous barrier prevents the movement of intermediate- and high molecular weight substances into the posterior chamber, while other substances are actively transported into the posterior chamber and establish osmotic gradient. Breakdown of the blood aqueous barrier reduces the efficiency of the osmotic gradient, which leads to a reduction in aqueous flow.

Clinical Relevance

Breakdown of the barrier is seen in patient's eyes with inflammation from uveitis or injury.

Cross-References

▶ Blood-Retina Barrier
▶ Retinal Blood Vessels

Further Reading

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Blood-Retina Barrier

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Definition

The blood retinal barrier results from the relationship between the retinal capillaries and the retinal pigment epithelium. It is responsible for homeostasis of the retina.

Structure

The blood-retinal barrier is located on the endothelial cells of the retinal capillaries. The endothelial cells are connected to each other by tight junctions. An extensive network of zonulae occludentes is present around the endothelial cells and the apicolateral aspect the RPE cells.

Function

The barrier prevents water-soluble molecules from entering the retina. It blocks macromolecules from the lumen toward the interstitial space and prevents diffusion of molecules in the opposite direction. The non-leaky tight junctions are associated with active transport of organic anions and glucose in the retinal vessels.

Clinical Relevance

Evidence of blood-retina barrier breakdown is seen as leaking on fluorescein angiogram. Disruption of this barrier is seen in the presence of diabetic retinopathy in the form of retinal edema and exudates. Other causes of barrier breakdown are hypertensive retinopathy, retinal vein obstruction, retinal ischemia, posterior uveitis, pars planitis, retinal vasculitis, coats disease, and retinoblastoma.

Cross-References

- ▶ Choroidal and/or Ciliary Body and/or Iris Melanoma
- ▶ Diabetic Retinopathy
- ▶ Fluorescein, as Diagnostic Agent
- ▶ Retinal Blood Vessels

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Blowout Fractures

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Synonyms

Floor fracture; Maxillary roof fracture; Orbital floor fracture

Definition

A blowout fracture, or orbital floor fracture, is an isolated fracture of the maxillary and/or palatine bones of the orbital floor with an intact orbital rim, usually caused by blunt trauma to the inferior orbital rim (Holck and Ng 2006).

Etiology

Motor vehicle accidents, interpersonal altercations, assaults, falls, sports-related injuries.

Clinical Presentation

Orbital floor fractures may be associated with life-threatening injuries and damage to the eyeball. Once these injuries are ruled out, attention can be directed to the clinical examination of the floor fracture (Lelli et al. 2007). Patients may present with periocular ecchymoses and edema, pain with eye movements, facial numbness, double vision, and blurred vision. Ophthalmic examination initially focuses on ruling out globe damage. Once achieved, a focused oculoplastic examination often shows extraocular motility disturbance, with vertical misalignment most common. Hypoesthesia in the region of the infraorbital nerve distribution is common. Enophthalmos may be seen, but often in the acute setting, patients are not enophthalmic secondary to periocular and periorbital edema and ecchymoses. Occasionally, an associated rim fracture may be palpable as a step-off deformity; periocular emphysema is a less common examination finding.

Diagnostics

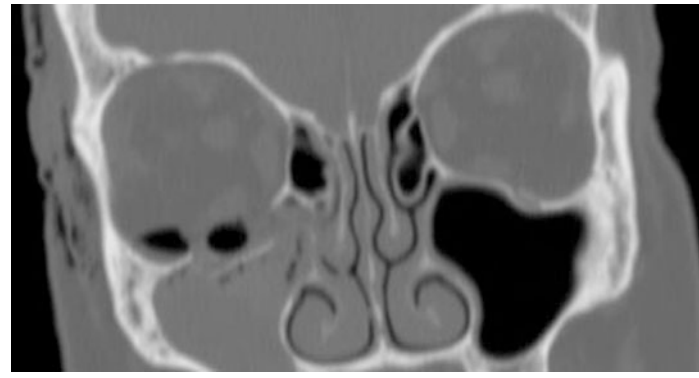
Facial fractures often occur as the result of significant trauma, and evaluation should begin with airway control and hemodynamic stabilization (Scherer et al. 1989; Mohammadi and Mohabbi 2007). Spinal cord injury should be ruled out. A thorough history and physical, including a complete head, neck, and ophthalmic, exam may then be performed. Orbital CT scanning with direct coronal imaging is considered the modality of choice for diagnosis of blowout fractures (see Fig. 1).

Differential Diagnosis

Zygomaticomaxillary (ZMC) complex fracture, medial orbital wall fracture, orbital hematoma, naso-orbital-ethmoid fracture, LeFort fracture, and maxillary (Guerin) fracture.

Prophylaxis

The use of restraints, seat belts, and protective headgear can help prevent orbital fractures.



Blowout Fractures, Fig. 1 Coronal imaging of a right orbital floor fracture with a large displaced portion of maxillary bone in the maxillary sinus. Orbital emphysema is seen, as is hemorrhage within the maxillary sinus

Therapy

Many patients with small orbital floor fractures, or those with intact periosteum, may be followed conservatively. Urgent repair of orbital floor fractures is exceedingly rare, and is warranted in two conditions: (1) The "white-eyed" orbital floor fracture with entrapment of the inferior rectus in a trap-door fracture; or (2) an unresolved oculocardiac reflex with vital sign instability. If these two conditions are not met, orbital floor fracture repair can proceed, when indicated, after initial periocular swelling has subsided. Indications for non-emergent blowout fracture repair are (1) extraocular muscle abnormality with clinical (forced duction testing) or radiographic evidence of entrapment of the extraocular muscle or perimuscular tissue or (2) significant enophthalmos ($\geq$2 mm) or the risk of significant enophthalmos from a fracture involving greater than 50% of the orbital floor and orbital periosteum. Perioperative antibiotics should be considered in patients with orbital fractures. Fractures should be repaired after adequate decrease in initial posttraumatic swelling, preferably within 2 weeks of the injury. For those patients treated conservatively, close ophthalmic follow-up is recommended.

Prognosis

Long-term prognosis after repair of blowout fractures is excellent. Postoperative infection rates are low and generally resolve with oral antibiotics. A small percentage of patients may develop postoperative asymmetry, globe or eyelid malposition, or extra-ocular muscle abnormality requiring revision surgery.

Epidemiology

Orbital floor fractures are most common in males (80%) and are usually the result of assault with a blunt object or fist, followed by motor vehicle accidents and falls. The orbital floor is the most commonly fractured orbital wall.

Cross-References

- ▶ Abscesses, Orbital
- ▶ Guerin (Maxillary) Fracture
- ▶ Lateral Orbitotomy
- ▶ Le Fort Fractures
- ▶ Maxillary Nerve
- ▶ Naso-Orbital-Ethmoid Fractures
- ▶ Orbit, Inflammation of
- ▶ Spiral Computed Tomography, in Orbital Evaluation
- ▶ Superior Transverse Ligament
- ▶ Three-Dimensional Computed Tomography, in Orbital Evaluation
- ▶ Zygomatic Bone

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Blue Cone Monochromatism

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Synonyms

S-cone monochromacy; X-linked incomplete achromatopsia

Definition

Blue cone monochromatism (BCM) is characterized by the absence of long-wavelength-sensitive (L) and medium-wavelength-sensitive (M) cone function in the retina. Thus, color discrimination is severely impaired from birth, and vision is derived from the remaining preserved short-wavelength-sensitive (S) cones and rod photoreceptors.

BCM belongs to the heterogeneous group of cone dystrophies. It is congenital, shows an X-linked recessive inheritance, and is generally considered as a stationary cone dysfunction syndrome.

Etiology

The normal human visual system achieves color vision by comparing the rate of quantum catches in three classes of cones – the short (S)-wavelength-sensitive, medium (M)-wavelength-sensitive, and long (L)-wavelength-sensitive cones – which are maximally sensitive to light at 430 nm, 535 nm, and 565 nm, respectively. The L (red) and M (green) pigment genes are located on the X chromosome, while the S-cone (blue) pigment is encoded by a gene located on chromosome 7.

The L and M genes in the genomic array on Xq28 are situated in a head-to-tail tandem arrangement with a single L opsin gene in a 5′ position, followed by one or more M opsin genes. Approximately 25% of male Caucasians have a single M gene, while 50% have two M genes, and the remainder have three or more genes. Expression of the L and M genes is regulated by the locus control region (LCR), a conserved sequence situated roughly 3.5 kb upstream of the L gene. The LCR ensures that only one opsin gene in the array is expressed in a single cone photoreceptor. It has also been demonstrated that only the first two genes of the array are expressed in the retina. The L and M cone opsins are encoded by six-exon genes, which are highly homologous sharing 96% amino acid identity, while their homology to S-cone opsin and rod opsin is approximately 40%. The highly homologous L and M opsin genes are as a consequence predisposed to unequal intergenic and intragenic recombination.

Mutations in the L and M pigment gene array that result in the lack of functional L and M pigments, and thus inactivate the corresponding cones, have been identified in the majority of BCM. These mutations fall into three classes. In the first class (about 40% of cases), a normal L and M pigment gene array is inactivated by a deletion in the LCR. In the second class of mutations (about 60% of cases), the LCR is preserved, but changes within the L and M pigment gene array lead to loss of functional pigment production. This is due to a two-step mutation mechanism. The first step involves nonhomologous recombination between the L and M opsin genes, which reduces the number of genes in the opsin array to one. This step is followed by a single nucleotide sequence alteration (point mutation), which inactivates the residual gene. The most common BCM genotype in this class consists of a single inactivated L–M hybrid gene with a C203R mutation: thymine to cytosine transition at nucleotide 648, which results in a cysteine to arginine substitution at codon 203 (Cys203Arg), disrupts the folding of cone opsin molecules. A third class of mutation includes partial or complete deletion of an entire exon.

Clinical Presentation

BCM typically presents in infancy with reduced visual acuity (6/24 to 6/60), pendular nystagmus, photophobia, and normal fundi. Cone dysfunction is mostly stationary. The nystagmus often wanes with time. Eccentric fixation may be present, and myopia is common. Color discrimination depends upon the luminance of the task: at mesopic (dark-adapted) levels, they have rudimentary dichromatic color discrimination based upon a comparison of the quantum catches obtained by the rods and the S cones. Color discrimination deteriorates with increasing luminance.

Findings

BCM is typically a stationary cone dysfunction and presents with normal funduscopy. A few families with pigmentary macular disturbances have been reported, with subsequent deterioration of visual acuity and color vision.

A recent study used adaptive optics scanning laser ophthalmoscopy and spectral-domain optical coherence tomography (SD-OCT) in 11 subjects, with mutations in the L and M cone opsin genes. Significant disruption of retinal lamination and cone mosaic topography and significant macular thinning were demonstrated in all subjects. The four subjects with C203R mutations and one subject with exon 2 deletion presented a classical BCM phenotype. The subjects with C203R mutations showed more normal total and central subfield thickness; retinal thinning was restricted to the outer nuclear layer and Henle fiber layer, and focal disruption of the ellipsoid zone of the inner segment was evident in SD-OCT. The subject with exon 2 deletion showed parafoveal thinning of the inner retina as well.

Diagnosis

- X-linked recessive inheritance trait
- Full field electroretinography (ERG) demonstrates absent or profoundly reduced photopic ERG: the 30 Hz cone ERG cannot be detected, while single flash photopic ERG is often recordable, although small and delayed. S-cone ERG is well preserved. The rod-specific and maximal responses usually show no definite abnormality.
- Psychophysical testing of color vision suggests retained tritan discrimination. These tests include the Farnsworth–Munsell 100 Hue test, Berson color plates; Hardy, Rand, and Rittler (HRR) plates; and the standard and enlarged Mollon–Reffin (MR) Minimal test.

Differential Diagnosis

- Rod monochromatism (RM) – an absence of all functioning cone photoreceptors with visual perception depending almost exclusively on rods. The rod monochromat has markedly reduced visual acuity and total color blindness. BCM is distinguished from RM via psychophysical and electrophysiological testing. The photopic ERG is profoundly reduced in both, although the S-cone ERG is well preserved in BCM. Classification can also be aided by family history, because BCM is inherited as an X-linked recessive trait, whereas rod monochromacy shows autosomal recessive inheritance. Blue cone monochromats are reported to display fewer errors along the vertical axis in the Farnsworth 100 Hue test (fewer tritan errors), and they may also display protan-like ordering patterns on the Farnsworth D-15 compared to RM.
- Progressive cone dystrophies – onset is usually in childhood or early adult life. Patients show worsening of cone function with deteriorating visual acuity, photophobia, and color vision and often develop rod photoreceptor dysfunction in later life.

Prophylaxis

Prenatal diagnosis can be performed in families in which the responsible gene has been identified.

Therapy

There is currently no specific treatment for BCM.

Prognosis

BCM is generally accepted to be a stationary disorder. A small number of families, with slow progression of cone dysfunction, have been reported.

Epidemiology

Affects approximately 1 in 100,000

Cross-References

- ▶ Achromatopsia (Rod Monochromatism), Gene Defects Causing
- ▶ Cone Dystrophies/Degeneration
- ▶ Inherited Color Vision Defects

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Blue Nevus

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Synonyms

Congenital ocular melanocytosis; Melanosis oculi; Ocular melanosis

Definition

A congenital pigmentary lesion of the episclera caused by increased number of subepithelial melanocytes.

B

Etiology

Primarily congenital.

Clinical Presentation

Ocular melanocytosis is characterized by irregular diffuse or sectorial blue or slate-gray discoloration of the sclera and episclera. The lesions are deep, immobile, and almost invariably unilateral. Heterochromia iridis is often a predominant feature, with part or the entire affected iris being darker than the iris of the fellow eye. Also, the background fundus pigmentation is greater in the affected eye (Albert et al. 2008).

Half of patients with ocular melanocytosis have periocular pigmentation of the skin in the first and second dermatomes of the trigeminal nerve. The combination of ocular and periocular pigmentation is called oculodermal melanocytosis or nevus of Ota.

Patients with ocular melanocytosis are at increased risk of developing glaucoma secondary to hyperpigmentation and increase the outflow resistance through the trabecular meshwork; this occurs in 10% of patients with ocular melanocytosis. Affected patients with fair skin have an increased risk of developing malignant melanoma in the skin, conjunctiva, uvea, or orbit. The lifetime risk of uveal melanoma in a patient with ocular melanocytosis is 1 in 400, compared to 1 in 13,000 of general population. Also, a higher incidence of optic nerve melanocytoma in affected eyes has been recognized (Gonder et al. 1982).

Diagnosis

Based on clinical presentation and examination with slit-lamp bimicroscopy, fundus examination

should be done to exclude uveal melanoma. Investigations are not usually required unless the lesion is atypical or undergone changes where biopsy is indicated.

Differential Diagnosis

- Conjunctival nevus
- Primary acquired melanocytosis (PAM)
- Malignant melanoma
- Choroidal melanoma with scleral extension
- Scleral thinning

Therapy

Ocular melanocytosis is a benign condition that does not require treatment. However, because of increased incidence of glaucoma and uveal melanoma, patients should be carefully examined periodically for their entire life to look for uveal, orbital and brain melanoma, and development of glaucoma (Krachmer et al. 2011).

Prognosis

Morbidity and mortality are mainly due to the development of complications including glaucoma and the increased risk of developing uveal melanoma in the affected eye.

Epidemiology

Ocular melanocytosis is an uncommon condition that is usually present at birth. It is more common in the black, Hispanic, and Asian populations. There is no difference in prevalence between males and females (Shields and Shields 2007).

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Blue Sclera

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Definition

Blue sclera refers to thinning and subsequent transparency of scleral type I collagen, which allows increased visibility of underlying choroidal pigment, giving sclera a seemingly blue appearance. Osteogenesis imperfecta (OI) is a hereditary disorder of type I collagen production, and patients with this condition demonstrate a diffuse blue appearance to the sclera (Agarwal and Jacob 2010; Basak 2011).

Etiology

Blue sclera is the most consistent manifestation of OI, which results from a mutation in *COLIA1* and *COL1A2*, coding for type I procollagen. However, classifications of this condition (types IV–VI) have been identified with normal sclerae. This rare disorder is also associated with abnormal fragility of bones and deafness.

Brittle cornea, blue sclera, and red hair are associated with the brittle cornea syndrome, a condition that also presents with skeletal, dental, and skin abnormalities. A missense mutation in *ZNF469* has been found to be causative for disease.

Other underlying conditions associated with the formation of blue sclera include Ehlers-Danlos syndrome (type VI), pseudoxanthoma elasticum, cornea plana, peripheral sclerocornea, buphthalmos, keratoconus, keratoglobus, high myopia, ciliary/equatorial staphyloma, oculodermal melanocytosis, and microcornea. Rarely, blue sclera occurs with Hallermann-Streiff syndrome, Marfan syndrome, Turner syndrome, Cheney syndrome, Menkes syndrome, pyknodysostosis, brittle corneas, or ectodermal dysplasia.

Blue sclera may also occur in normal infants during the first several months of life; however, persistence of blue discoloration over time may suggest the presence of elevated intraocular pressure. Premature infants frequently demonstrate blue sclerae, particularly those of Caucasian origin.

Blue sclera may also occur in isolation as an inherited autosomal dominant or autosomal recessive anomaly (Hunt 2002; Hoyt and Taylor 2012).

Clinical Presentation

Blue sclera presents with a bluish appearance to the sclera and may be associated with pathologic or non-pathologic etiology. Other ocular characteristics of connective tissue disorders associated with blue sclera include thin cornea, epicanthal fold, myopia, keratoconus, and angioid streaks. Systemic characteristics of connective tissue disorders associated with blue sclera include skin abnormalities, cardiac abnormalities, kyphoscoliosis, joint hypermobility, fragile bones, hearing abnormalities, vascular abnormalities, and gastrointestinal abnormalities (Agarwal and Jacob 2010; Kanski and Bowling 2011).

Diagnosis

Diagnostic evaluation of blue sclera involves external examination, slit lamp biomicroscopy, and systemic evaluation for associated disorders. Although no definitive test exists for OI, genetic testing can confirm or exclude known mutations (Agarwal and Jacob 2010).

Differential Diagnosis

Pediatric and orthopedic evaluations should be considered to exclude inherited causes of blue sclera and to identify systemic manifestations of disease. For instance, brittle cornea syndrome is characterized by blue sclera, brittle cornea, and red hair.

Oculodermal melanocytosis is a congenital condition which results in a bluish hue to the episclera. Unlike typical congenital blue sclera, this is secondary to dysfunctional melanocyte migration and tends to be unilateral. Patients are not at risk for thinning such as in OI but are at increased risk of uveal melanoma and glaucoma.

Scleromalacia perforans, most frequently associated with rheumatoid arthritis, induces focal thinning of the sclera and a similar blue appearance due to visualization of the underlying sclera. This generally occurs at an older age and is focal, in contrast to the genetic etiology and diffuse effect of the aforementioned conditions (Basak 2011; Kanski and Bowling 2011).

Prophylaxis

No gene therapy is currently available. However, genetic counselling for associated inherited disorders may be beneficial for patients with blue sclera and other manifestations of systemic disease.

Therapy

Surgical intervention may be indicated in cases of extreme thinning and perforation. Structural support can be provided by a preserved scleral graft or autologous fascia lata, particularly in cases requiring suturing of a device such as a tube implant. Systemic investigations and treatment should be considered to address underlying pathology. Appropriate referrals to pediatric and orthopedic evaluations may be indicated for non-ocular manifestations (Kanski and Bowling 2011).

Prognosis

Prognosis varies with the presence of ocular and systemic manifestations of the underlying disorder. Patients with blue sclera are at increased risk for globe rupture or intraoperative scleral perforation during routine eye surgery. Systemic disorders are also prevalent in patients such as carotid-cavernous fistula, arterial rupture, hearing loss, and bone fractures (Agarwal and Jacob 2010; Basak 2011).

Epidemiology

Blue sclera is associated with systemic connective tissue disorders, most commonly osteogenesis imperfecta, which presents at approximately 1 in every 20,000 live births. Prevalence is relatively similar worldwide, with higher frequency reported in Zimbabwe. Brittle cornea syndrome, although rare, presents largely from the Middle East and North Africa and was identified primarily in consanguineous families of Tunisian-Jewish descent; it has since also been described in Europeans (Kanski and Bowling 2011).

Cross-References

- ▶ Connective Tissue Disease
- ▶ Cornea Plana
- ▶ Ectodermal Dysplasia
- ▶ Ehlers-Danlos Syndrome, Gene Linkage of Disease
- ▶ Osteogenesis Imperfecta, Blue Sclera
- ▶ Staphylomas, Congenital, Anterior

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Blunt Trauma

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A blunt ocular trauma is defined as eye trauma by an object that does not penetrate the eye; the trauma may damage the structures at the anterior segment of the eye (the eyelid, conjunctiva, sclera, cornea, iris, and lens) and those at the posterior segment of the eye (retina and optic nerve) as well as surrounding structures of the orbital bones and the sinuses. The most devastating injury from ocular blunt trauma is open-globe rupture caused by suddenly elevating intraocular pressure; the ruptures are typically at the site of greatest structural weakness near the equator, at the limbus, and directly behind the insertion of the rectus muscles.

A blunt ocular injury can be due to any high-velocity objects. The most common blunt objects reported by May et al. from the US Eye injury Registry were rocks, fists, baseballs, lumber, and fishing weights. A blunt ocular injury can be due to any high-velocity objects including rocks, fists, baseballs, and lumber.

Risk Factors

Male gender is a predominant risk factor for ocular trauma as well as sport occupation and the use of power tools in the home environment.

Evaluation and Diagnosis

Assessment of a patient after ocular trauma should include complete history such as when and where the injury occur, what was the mechanism of the injury, what was the offending object, do the patient wore eye protection or glass, when was the patients last oral intake, and what was the eye status before the injury including previous ocular surgeries.

Ophthalmic examination can be difficult after an eye trauma; the injured eyes may be very swollen and difficult to open; in patients with a high likelihood of scleral rupture, the clinician should avoid

any examination procedure that might apply pressure to the eyeball, such as eyelid retraction or intraocular pressure measurement by tonometry.

The ophthalmic examination should include visual acuity, relative afferent pupillary defect, extraocular movements, palpation of orbital rim for step-off fractures and subcutaneous emphysema, sensation of the V1 and V2 on the forehead and cheek, measuring the degree of proptosis or enophthalmos, careful slit lamp examination of anterior segment, and a dilated fundus examination.

Imaging should include head and orbit axial and coronal computed tomography (CT) without contrast, utilizing 1–2 mm cuts. Ultrasound examination may be useful in the eyes with opaque media; although it may be necessary to defer ultrasonography until a scleral rupture is excluded, magnetic resonance imaging (MRI) can be a useful imaging modality for detecting intraocular foreign bodies made of wood, plastic, or stone but must be avoided when high suspicion of metal foreign bodies exists.

Clinical Findings

Subconjunctival Hemorrhage

The conjunctiva contains many small and fragile blood vessels; any eye trauma can cause bleeding underneath the conjunctiva from these small blood vessels, causing a solid red patch of blood on the white of the eye. The presence of subconjunctival hemorrhage, particularly with 360° of bullous SCH, can mask a scleral laceration and therefore must raise high suspicion of globe rupture.

Hyphema

Blood accumulating in the anterior chamber of the eye (the space between the cornea and the iris) called hyphema usually results from marked elevation in intraocular pressure with sudden distortion of intraocular structures and bleeding from blood vessels supplying blood to the iris, ciliary body, and angle structures.

The three most common complications from hyphema are elevated intraocular pressure, rebleeding at 4–6 days after the event, and corneal blood staining.

Angle Recession

The angle is located between the peripheral cornea and the peripheral iris. The angle contains the trabecular meshwork, which acts as a filtration system for the aqueous fluid draining from the eye. Angle recession is a common sequela of blunt ocular trauma and characterized by a variable degree of cleavage between the circular and the longitudinal fibers of the ciliary muscle. The angle of the eye can be visualized through a procedure known as gonioscopy.

Vitreous Hemorrhage

Traumatic vitreous hemorrhage can occur in the setting of blunt ocular trauma; the causes for bleeding into the vitreous cavity are rupture of blood vessels of the iris, ciliary body, retina choroid, and sclera; in this setting ultrasound examination is indicated for the detection of the cause for the bleeding and to rule out retinal tear, retinal detachment, and scleral rupture.

Macular Hole

Posttraumatic macular hole can be seen after a blunt trauma; the mechanisms for this complication are vitreous traction, severe berlins edema, subretinal hemorrhage caused by choroidal rupture, and contusion necrosis in the fovea. The macular hole can be seen immediately after the trauma or within days and even weeks.

Commotio Retinae

A disruption in the photoreceptor outer segment, characterized by gray-white discoloration of the outer retina. It can occur centrally or peripherally, and when it involves the macula, it is called Berlin's edema; usually there is no leakage of fluid and therefore it is not considered a true edema. When it involves the macula, a severe decrease in visual acuity can occur; fortunately, the prognosis for visual recovery is good and these changes gradually resolve spontaneously.

Choroidal Rupture

Blunt trauma causing mechanical compression of the eyeball in the anterior–posterior axis with concomitant rapid hyperextension in the horizontal axis. The sclera's tensile strength and retinal

elasticity resist this compression. However, Bruch membrane breaks because it does not have sufficient tensile strength or elasticity and with it a disruption in the choriocapillaris and the RPE occurs. Over time, choroidal neovascularization can develop.

Initial Treatment

Treatment in the emergency room for a known globe rupture or in highly suspicious cases includes avoidance of further examination or manipulation and the placement of a protective eye shield to prevent accidental pressure on the globe. The patient should be kept with nothing by mouth and a tetanus injection given as needed. Antiemetics should be given if the patient is nauseated. Broad-spectrum IV antibiotics should be instituted.

Borrelia burgdorferi

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Definition

Borrelia burgdorferi is a spiral-shaped (spirochete) bacterium that is endemic in North America and Europe. It is neither gram negative nor gram positive, and it is most commonly known as the causative agent of Lyme disease.

Microbiology

Borrelia burgdorferi is a spiral-shaped, microaerophilic two-membrane bacterium that is primarily extracellular. *B. burgdorferi* is one of the few pathogenic bacteria that can survive without iron, instead requiring manganese for proper function of some of its enzymes. The bacterium is covered with flagella and peptidoglycan and can be mistaken for a gram-negative organism because of its double membrane.

The *B. burgdorferi* genome contains 21 plasmids, more than any other known bacterium. The outer membrane is composed of various unique outer-surface proteins (Osp) that are presumed to play a role in virulence.

Transmission and Life Cycle

The bacterium is predominantly transmitted to humans by the *Ixodes* tick, and these ticks, typically in the larval stage, become infected with the spirochete after feeding on infected rodents (mice are the preferred host). Once mature, deer are the preferred host, but the *Ixodes* ticks cannot become infected from deer. Humans can become infected after being bitten by an infected tick.

Clinical

B. burgdorferi is primarily known for causing Lyme disease. Early symptoms can include fever, headache, fatigue, and the characteristic "bull's eye" rash (erythema migrans) on the skin. Later symptoms can include myocarditis, cardiomyopathy, arrhythmia, radiculopathy, arthritis, arthralgia, meningitis, neuropathies, hearing loss, and facial nerve palsies. If left untreated, patients may develop permanent neurological deficits.

Optic nerve involvement is considered rare in the context of Lyme disease but can occur if the

patient develops neuroborreliosis, a condition in which the infection affects the central nervous system. Interestingly, *B. burgdorferi* has also been linked to non-Hodgkin lymphomas.

Diagnosis

The diagnosis of Lyme disease is based upon clinical history and epidemiological risk of exposure to *Ixodes* ticks. For a patient with disseminated disease, serological testing is used to confirm the diagnosis. Serological testing involves an ELISA screening followed by a confirmatory Western blot. Centers for Disease Control and Prevention (CDC) criteria require five or more specific bands for IgG and two or more different bands for IgM.

Treatment

Because *B. burgdorferi* is microaerophilic, it grows slowly and requires the use of longer treatment courses, predominantly with doxycycline.

Cross-References

► Lyme Disease

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Botox: Spastic Entropion

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Synonyms

Overriding orbicularis

Definition

Spastic entropion results from ocular irritation or inflammation which then triggers sustained orbicularis muscle contraction and inward rotation of the eyelid margin.

Indication

Spastic entropion that is causing corneal irritation, which then exacerbates the orbicularis spasm and perpetuates the irritation/entropion cycle.

Contraindication

Eyelids with underlying involutional changes that require definitive surgical repair.

Techniques and Principles

Botulinum toxin type A is injected subcutaneously into the overriding preseptal orbicularis muscle to relieve the spasm. A total of 5–10 U of botulinum toxin type A may be divided between two injection sites, one medial and one lateral. The underlying cause of the ocular irritation or inflammation must also be treated to eliminate the trigger for the orbicularis spasm.

Outcome

Botulinum toxin type A takes 48–72 h to have an effect and can last an average of 3–4 months.

When used in the treatment of spastic entropion, a single treatment is usually sufficient to break the irritation/entropion cycle and return the lid to its normal anatomic position, as long as the underlying cause of the ocular irritation is treated as well.

Complications

Excessive relaxation or paralysis of the orbicularis muscle may cause a loss of orbicularis tone and result in an ectropion. Deeper injection into the postseptal space may allow diffusion of the toxin to the lower lid retractors, resulting in reverse ptosis, or to the extraocular muscles, resulting in diplopia. These complications will resolve as the effect of the toxin dissipates.

Cross-References

► Congenital Entropion

Further Reading

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Bowen's Disease

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Synonyms

Intraepidermal carcinoma; Squamous carcinoma in situ

Definition

Bowen's disease is a squamous carcinoma in situ of the skin. This premalignant squamous lesion may progress to invasive squamous cell carcinoma in less than 5% of patients.

Etiology

Bowen's disease occurs in the keratin-producing cells of the epidermis and respects the basement membrane. It is encountered in elderly, fair-skinned individuals with a history of chronic sun exposure. Other risk factors include arsenic exposure and the human papillomavirus.

In the past, Bowen's disease was thought to have an association with primary internal malignancies; however, current evidence does not support this hypothesis (Reizner et al. 1994; Shields and Shields 1999; Cox et al. 2007; Albert and Jakobiec 2008).

Clinical Presentation

Presents as velvety, scaly, erythematous plaques with well-defined borders on sun-exposed areas. The lesions are asymptomatic and slow growing. Bowen's disease presents as a single lesion in two thirds of cases.

Diagnostics

Definitive diagnosis is determined with excisional biopsy. Histolopathologically, Bowen's disease demonstrates hyperkeratosis, parakeratosis, acanthosis, and dysplasia within the full thickness of the epidermis (Shields and Shields 1999; Albert and Jakobiec 2008).

Differential Diagnosis

Actinic keratosis
Squamous cell carcinoma
Keratoacanthoma
Paget disease
Lichen simplex

Benign lichenoid keratosis
Tinea corporis
Eczema
Psoriasis, plaque

Prophylaxis

Patient should have a complete skin examination of sun-exposed areas and counseled to avoid sun exposure. Routine screening of these patients is necessary to avoid delay in treatment of additional lesions.

Therapy

Complete surgical excision is recommended to rule out squamous cell carcinoma. For smaller lesions, 4 mm margins are recommended. Frozen sections or Mohs micrographic surgery are alternative techniques for larger, recurrent lesions in critical areas. Other treatments include radiation, cryotherapy, photodynamic therapy, and topical chemotherapy. Observation can be offered in patients with short life expectancy or small lesions not suspected to progress to invasive squamous cell carcinoma rapidly (Shields and Shields 1999; Cox et al. 2007; Albert and Jakobiec 2008).

Prognosis

Prognosis is good, with less than 5% of cases advancing to invasive squamous cell carcinoma.

Epidemiology

More commonly observed in Caucasians in sun-exposed regions. Incidence has been reported to be 14 cases per 100,000 whites in Minnesota in 1991 and 142 cases per 100,000 whites in Hawaii in 1994 (Reizner et al. 1994; Shields and Shields 1999; Albert and Jakobiec 2008).

Cross-References

- ▶ Actinic Keratosis
- ▶ Carcinoma In Situ, of Conjunctiva
- ▶ Keratoacanthoma
- ▶ Squamous Cell Carcinoma of Eyelid

References

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Breakup Time (BUT)

▶ Tear Breakup Time

Bridge Flap Technique

▶ Cutler-Beard Procedure

Bright-Flash Electroretinogram

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Synonyms

The electrical response of the retina to a light flash of very high intensity (energy)

Definition

The electroretinogram (ERG) is the electrical mass response of the retina to a light stimulus and is commonly used to objectively measure global retinal function. In clinical practice, ERG serves to identify disorders of retinal function in patients complaining of visual disturbances, to monitor progression of retinal degenerative diseases, and to assess the response to treatment in maintaining retinal function. Bright-flash electroretinogram (bright-flash ERG) refers to the recording of the electroretinogram in the dark-adapted state using a very bright flash of light to elicit a response of maximal amplitude.

Of note, a distinction should be made between the retinal response to bright light measured as a routine part of the standard ERG testing protocol and the bright-flash ERG discussed here, which refers to the electrical response of the retina to a super bright-light stimulus.

Purpose

Bright-flash ERG testing is beneficial in cases of dense media opacity where light transmission to the retina through the ocular media is diminished or when retinal function is minimal such that intense light exposure is required to elicit a measureable response (Fuller et al. 1975; Wendel et al. 1984).

Otherwise, under most physiological and disease conditions tested in routine clinical practice, sufficient information regarding retinal function is achieved with the standard ERG protocol without the need to use very bright flashes of white light for ERG recording. Furthermore, the light intensity employed for this test, even though brief, is often uncomfortable for the patient. Lastly, not all commercial or assembled electrophysiological systems, currently available for ERG recording, are furnished to deliver sufficiently bright white-light stimulus.

Principle

Bright-flash ERG is recorded with differential amplifiers using three electrodes: a corneal active electrode, a reference electrode, and a ground electrode. Additional essential component for bright-flash ERG recording is a Ganzfeld light source that can deliver a sufficiently bright-light stimulus (minimum energy 300 cd-s/m^2). For recording electrode, a bipolar corneal electrode is needed that will not generate a photoelectric artifact in response to the bright-light stimulus.

Indication

Bright-flash ERG can be beneficial in the following cases:

1. Opaque optical media: In cases of severe ocular media opacity (e.g., opaque cornea, hypermature cataract, dense vitreous hemorrhage, etc.), light transmission to the retina is minimal such that the standard ERG response may be non-recordable. In these cases, when an assessment of retinal function is needed, using a very bright white-light stimulus often allows sufficient light to reach the retina and to elicit a recordable ERG response. Even though often of subnormal amplitude, such a response can provide helpful information about the functional status of the retina (Fuller et al. 1975; Wendel et al. 1984).
2. Candidates for implantation of retinal neuroprosthesis: Electrical neuroprosthetic devices have been developed and approved for clinical use in blind patients suffering from advanced retinitis pigmentosa. A bright-flash ERG can be used in these candidates in order to verify the extent to which retinal function has been lost.
3. Assessing photoreceptor pathology: Inherited retinal degenerations are a group of disorders caused by a mutation of a gene, encoding a protein which is specific to photoreceptors, RPE, or extracellular matrix. To date, more than 200 genes are known to cause photoreceptors degeneration. Although many inherited retinal degenerations share a similar phenotype, they differ in the underlying pathological mechanism leading to photoreceptors apoptosis and loss of vision. The bright-flash ERG elicits a

maximal, saturated a-wave that can be used to assess the underlying pathological mechanism/s of photoreceptors loss of function. Although currently this information is used mainly for experimental purposes, it is expected to become a valuable measure of retinal function in future clinical trials assessing the response to treatments targeting specific gene mutations (Cideciyan 2000; Hood and Birch 2006).

4. Monitoring of response treatment: When treatments for specific photoreceptors degenerative diseases will be developed, their efficacy will need to be assessed. Measurements of visual acuity and visual fields are subjective, while ERG recording is objective. Bright-flash ERG is an option to record the remaining retinal function of patients in advanced degenerative stage before treatment and during treatment to document treatment efficacy.

Contraindication

The intensely bright flash can elicit a substantial photoelectric artifact when using monopolar recording with corneal electrodes such as DTL electrode or with skin electrodes. This artifact can mask the actual ERG. Therefore, bright-flash ERG cannot be recorded in patients that cannot tolerate a bipolar corneal electrode or when there are contraindications for the use of such electrode, e.g., corneal abrasion, severe external eye infection, etc.

Advantage/Disadvantage

Advantage: assessment of minimal remaining retinal function, can be used with opaque optical media, indicate mechanism of photoreceptors loss of function.

Disadvantage: very bright and uncomfortable for the patient.

Cross-References

- ▶ Cataract, Causes and Treatment
- ▶ Diabetic Retinopathy, Proliferative
- ▶ Electroretinogram
- ▶ Ocular Prostheses
- ▶ Retinitis

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Brightness (Radiance)

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Synonyms

Radiance

Definition

Brightness L_e [$Wsr^{-1}\ m^{-2}$] is a radiometric measure of the amount of radiant power Φ_e [W] that is emitted from a surface with specified area A [m^2] within a given solid angle Ω [sr] into the specified direction angle ε. It is used to measure radiation emitted by a surface that can be received by the eye looking from angle ε. A lambertian radiator emits with homogeneous brightness which is independent of the angle of observation ε.

The definition of radiance $L_e \equiv \frac{\delta^2 \Phi_e}{\delta \Omega dA \cos \varepsilon}$.

Cross-References

- ▶ Illuminance: Definition
- ▶ Luminance: Definition

Brow Fat Pad, Superior Extension of the Sub-brow Fat Pad

- ▶ Retro-Orbicularis Oculi Fat (ROOF)

Bruch's Membrane

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Synonyms

Vitreous lamina (*lamina vitrea*)

Definition

Named after the German anatomist Karl Wilhelm Ludwig Bruch, it is the inner most layer of the choroid and is responsible for establishing the blood-retinal barrier. It is about 2 μm thick and consists of five sublayers: basement membrane of the pigment epithelial cells, the inner collagen fiber layer, an elastic fiber sheet, the outer collagen fiber layer, and the basement membrane of the choriocapillaris.

Cross-References

- ▶ Age-Related Macular Degeneration
- ▶ Blood-Aqueous Barrier
- ▶ Blood-Retina Barrier
- ▶ Choroid, Gyrate Atrophy of
- ▶ Drusen
- ▶ Retinal Pigment Epithelium

Buccal Mucous Membrane Graft

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Synonyms

Mucosal graft

Definition

Free mucosal tissue graft transplanted from the oral cavity to the eyelid as a conjunctival substitute.

Indication

Used during eyelid reconstruction surgery when there is posterior lamellar, in particular, conjunctival inadequacy. Tissue loss may be secondary to cancer resection surgery (including Mohs surgery), trauma, cicatricial changes, or congenital inadequacy.

Contraindication

Patients with significant oral disease or extensive prior oral surgery on mucosal surfaces may not be adequate donors. Graft size is limited anatomically and assurance must be given to spare the region of Stensen's duct.

Techniques and Principles

Assessment of the degree of conjunctival loss or foreshortening is performed and the proper graft

size determined. Potential donor sites for buccal mucosal tissue include the mucosal surfaces of the lower and upper lip (avoiding the midline frenula) and the lateral walls of the oral cavity (avoiding the area surrounding Stensen's duct). The graft is harvested by first creating an incision with a #15 Bard-Parker blade and the mucosa removed with Stevens scissors. The graft should be harvested as thin as possible, without creating buttonholes, to avoid deeper unnecessary submucosal dissection. The oral cavity wound is left to heal by secondary intention. The graft is further thinned if necessary and sutured into the conjunctival defect with absorbing gut suture.

Outcome

Once the graft has taken, in approximately 7 days time, it provides an excellent substitute for conjunctiva in both function and appearance. Some degree of graft contracture can be anticipated over the following several weeks.

Complications

Graft failure and slough with failure to reconstruct the conjunctival surface are possible. Donor site complications include potential infection, injury to Stensen's duct, and contracture and phimosis of the oral mucosal lining.

Cross-References

► Eyelid Reconstruction

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Bulla

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Synonyms

Bullous keratopathy; Epithelial edema; Microcystic edema

Definition

Bullae, or bullous keratopathy, refer to the condition in which excess fluid accumulates within or between corneal epithelial cells, causing disruption of the normal corneal epithelial architecture and the formation of epithelial blisters or cystic spaces. The loss of a smooth epithelial surface results in scattering of light and loss of vision. The fluid-filled bullae can shift or rupture to cause pain and foreign body sensation and may become secondarily infected, resulting in microbial keratitis. Patients with bullous keratopathy will complain of various levels of eye discomfort, decreased visual acuity, loss of contrast, glare, and photophobia Krachmer et al. (2011).

Etiology

The two common causes of corneal epithelial edema are endothelial dysfunction and epithelial hypoxia or trauma. Corneal transparency is reliant on a high density of functional endothelial cells to maintain the cornea in a dehydrated state. Endothelial dysfunction leads to stromal edema. Stromal edema occurs when the corneal water content exceeds 78% and is manifested as a thickened cornea with gray, ground-glass haze. Stromal swelling can displace the epithelial basement membrane and Descemet's membrane, causing

folds called *shift lines* and *corneal striae*, respectively. If stromal edema is chronic and advanced, subsequent epithelial edema with bulla formation ensues.

Endothelial dysfunction can be the result of Fuchs' endothelial corneal dystrophy, a disorder that causes bilateral, progressive corneal endothelial cell loss and dysfunction. Gradual edema and subsequent opacification of the cornea in Fuchs' endothelial corneal dystrophy typically results in symptomatic loss of visual acuity between the ages of 40 and 50. Other types of primary corneal endothelial failure include congenital hereditary endothelial dystrophy, posterior polymorphous dystrophy, and iridocorneal endothelial syndrome. Endothelial dysfunction can also result from an infectious or inflammatory condition, such as in herpetic or cytomegaloviral corneal endotheliitis. Intraocular surgery, particularly cataract surgery, is an important cause of direct endothelial injury, which can result in generalized endothelial dysfunction, particularly in patients predisposed to endothelial dysfunction or with preoperative endothelial cell counts Suh et al. (2008). Laser iridotomy used for the treatment or prevention of angle closure glaucoma can be complicated by corneal endothelial trauma and subsequent bullous keratopathy. Sudden rises in intraocular pressure can result in stromal edema and secondary epithelial microcystic edema due to overwhelming the ability of the corneal endothelium to maintain stromal dehydration. In patients who have undergone corneal transplantation, endothelial cell loss in the graft tissue results in stromal edema and subsequent epithelial edema.

Contact lens overuse or poor contact lens fit can lead to epithelial hypoxia, hypercapnia, or trauma, all of which can subsequently result in intracellular epithelial edema.

Occurrence

Bullous keratopathy secondary to cataract surgery is among the most common indications for corneal transplantation worldwide. In a review of indications for penetrating keratoplasty in a large US academic institution, pseudophakic bullous keratopathy was the leading indication for penetrating keratoplasty and accounted for 22.9–28.4% of penetrating keratoplasties performed in each 5–7 year interval between 1983 and 2005.

The prevalence of Fuchs' endothelial dystrophy is difficult to assess given its later onset and lack of symptoms in the early stage; however, it accounts for a significant proportion of corneal transplantations performed in the United States, up to 29% in some studies and 10.8–16.3% in the aforementioned study of penetrating keratoplasties between 1980 and 2005 Ghosheh et al. (2008).

Bullous keratopathy after laser peripheral iridotomy is a rarely reported complication. However, in a nationwide study of Japanese patients, laser peripheral iridotomy was the second leading cause of bullous keratopathy in patients undergoing keratoplasty, accounting for 23.4% of cases. Cataract surgery was the leading cause, associated with 44.4% of cases Shimazaki (2007).

Classification

Bullous keratopathy as a complication of cataract removal can be classified as *pseudophakic bullous keratopathy* if an intraocular lens implant is in place or *aphakic bullous keratopathy* if the patient is aphakic.

Epithelial bullae are associated with stage III and stage IV Fuchs endothelial dystrophy.

Epithelial edema with microcysts rather than larger bullae, often associated with acutely elevated intraocular pressure, is usually referred to as microcystic edema.

Cross-References

- ▶ Endothelial Failure
- ▶ Fuchs' Dystrophy Disease
- ▶ Primary Endothelial Failure, after Penetrating Keratoplasty

References

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Bullous Keratopathy

► Bulla

Buried Disc Drusen

► Pseudopapilledema: Disc Drusen

Burns

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Definition

Thermal, electrical, or chemical injury to the eyelids, adnexal structures, and/or ocular surface, resulting in soft tissue damage (management of chemical injuries is discussed elsewhere).

Etiology

Scald burns from hot water are the most common cause of thermal injury to the periocular region. Children, the elderly, and seizure sufferers are particularly vulnerable. Flame injuries are more likely to be seen in an occupational context and typically cause deeper burns. Electricity may cause arc, flash, and/or flame burns. Other sources include sunburns, motor vehicle accidents, house fires, and propane tank explosions.

Clinical Presentation

Clinical manifestations depend on the structures involved and severity of the burn. Eyelid skin is among the thinnest in the body, and deeper burns occur easily. First-degree burns involve only the dermis. They present with erythema and superficial blistering that typically heals within 1 week. Second-degree burns involve a variable depth of dermis. More superficial insults create painful, fluid-filled blisters with a moist red base. Healing occurs within 2 weeks with minimal scarring. Deeper insults result in blisters with a pale or mottled base; healing often requires 3 weeks or more and is accompanied by significant scarring and contraction. Third-degree burns involve the full epidermal-dermal thickness. Sensation is lost due to destruction of nerve fibers, and healing occurs only peripherally due to coagulation of the dermal blood vessels. Fourth-degree burns also involve the underlying muscle, bone, and/or vital structures.

Fortunately, thermal injuries rarely damage the ocular surface primarily. A variety of mechanisms, including a 150 ms reflex blink, Bell's phenomenon, and reflex protective movements of the head and arms, decrease this risk. Most damage arises secondarily, due to lagophthalmos and exposure from cicatricial ectropion or other eyelid deformities. Fluid resuscitation, sedation, and mechanical ventilation often exacerbate lagophthalmos via chemosis and loss of orbicularis tone.

Facial burns also raise the specter of laryngeal edema from smoke inhalation. There should be a low threshold to secure the airway and initiate mechanical ventilation.

Diagnosis

Diagnosis is based on history and exam. Careful inspection of the eyelids, brow and eyelash hairs, ocular surface, and fornices is paramount. Fluorescein and cobalt blue light are critical for assessing integrity of the ocular surface.

Differential Diagnosis

Bullous pemphigoid
Pemphigus vulgaris
Toxic epidermal necrolysis
Blistering drug eruptions
Photosensitivity reactions

Prophylaxis

Occupational, motor vehicle, and home safety measures.

Therapy

Therapy is directed toward protecting and/or reestablishing the integrity of the ocular surface. Restoring function to the eyelids is an important but secondary goal. Aggressive lubrication should be initiated early, and antibiotics covering *Pseudomonas* should be added if punctate staining or epithelial defects are present. Elevating the head of the bed may reduce chemosis and periocular edema. Orbital compartment syndrome is occasionally seen in patients receiving massive volume resuscitation for burns involving a large percentage of the body surface area. Standard canthotomy/cantholysis should be performed in these cases. Eschar should be debrided, and raw tissues protected with emollients and occlusive dressings. Moisture chambers are rarely effective in the face of significant lagophthalmos, and temporary suture tarsorrhaphy should be performed immediately in response to ocular surface decompensation. The timing of skin grafting to correct cicatricial ectropion is controversial, but recent evidence suggests benefit from intervention within the first week.

Prognosis

Prognosis is highly variable depending of the severity of injury.

Epidemiology

Up to one quarter of patients admitted to burn units have eyelid involvement.

Cross-References

- ▶ Desquamating Skin Conditions
- ▶ Exposure Keratitis/Keratopathy
- ▶ Lagophthalmos
- ▶ Thermal Injury: Overview

Further Reading

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Calcific Band Keratopathy

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Synonyms

Band keratopathy; Calcific keratopathy; Calcium hydroxyapatite deposition

Definition

First described by Dixon in 1948, calcific band keratopathy refers to calcific degeneration, often in a "band"-like distribution, of the superficial cornea that mainly involves the Bowman layer and the anterior stroma. Involvement often begins in the interpalpebral region and is initially characterized by fine, dust-like deposits that are basophilic on H&E pathology staining, usually with a clear zone between the limbus and the border of the deposition. Over time, the deposits can coalesce to form dense calcific plaques that can obscure the visual axis. Scattered "holes" throughout the band are thought to occur at sites where corneal nerves penetrate Bowman's layer. Elevation of the epithelium secondary to extensive and irregular calcium deposition can result in pain, photophobia, foreign body sensation, recurrent corneal erosions, and decreased vision or glare.

Etiology

While calcific band keratopathy can be idiopathic, the major known causes fall into the categories below:

1. **Chronic ocular diseases**, especially intraocular inflammation, can lead to band keratopathy. Examples include chronic uveitis associated with juvenile idiopathic arthritis, interstitial keratitis, severe dry eye and corneal exposure syndromes, phthisis bulbi, long-standing glaucoma, spheroidal keratopathy, and the presence of a keratoprosthesis.
2. **Hypercalcemia** associated with the following conditions: hyperparathyroidism, vitamin D toxicity (e.g., sarcoidosis, oral intake, and osteoporosis), milk–alkali syndrome, renal failure (e.g., Fanconi syndrome), hypophosphatasia, multiple myeloma, carcinoma metastatic to the bone, and Paget's disease.
3. **Hyperphosphatemia** with normal levels of serum calcium, as can occur in some patients suffering from renal failure.
4. **Systemic diseases** such as gout, discoid lupus, tuberous sclerosis, and Norrie disease.
5. **Chemical exposure**, such as with the chronic use of older glaucoma medications or dry-eye drops with mercury-derived preservatives (phenylmercuric nitrate or acetate), can also lead to calcific band keratopathy. Others include silicone oil in an aphakic eye, exposure to mercury fumes, and phosphate-containing drops.

U. Schmidt-Erfurth, T. Kohnen (eds.), *Encyclopedia of Ophthalmology*,
https://doi.org/10.1007/978-3-540-69000-9

6. **Hereditary** transmission of calcific band keratopathy has also been reported, occurring in an autosomal recessive fashion. Thus far, only the human NBC1 (sodium-bicarbonate co-transporter one) gene has been implicated in band keratopathy, mutations of which result in severe ocular and renal dysfunction (band keratopathy, cataracts, and proximal renal tubular acidosis).

Classification

While calcific band keratopathy can vary in the distribution and severity of deposition, there have not been literature reports of consistent differences in the characteristics of calcific keratopathy based on etiology or other factors.

Management

The most appropriate first step in the management of calcific band keratopathy is to conduct workup, such as serum electrolytes and urinalysis, to assess for the presence of systemic metabolic or renal disease, especially if there is no clear ocular cause for the keratopathy. Consequently, underlying ocular and systemic conditions should be treated or controlled to the extent possible to prevent the progression or recurrence of the keratopathy.

Indications for treating band keratopathy mainly include vision impairment and physical discomfort. With extensive calcium deposition, mechanical removal may be helpful and is widely used in parts of the developing world as the primary treatment method given the ease of surgery and minimal cost involved. Chelation with disodium ethylenediaminetetraacetic acid (EDTA) remains the mainstay of therapy, especially in the developed world; please refer to the separate section on "Chelation Therapy, for Calcific Band Keratopathy" for further discussion of this method. The ability to control the depth and area of ablation with excimer laser phototherapeutic keratectomy (PTK) can make it a useful modality of treatment in calcific band keratopathy, especially if residual opacification remains after initial EDTA chelation. However, since calcium ablates at a different rate from corneal stroma, PTK can result in an irregular surface. A masking agent to protect normal tissue may help achieve a smoother corneal surface post-ablation. Amniotic membrane transplantation (AMT) may also be used in the treatment of band keratopathy, usually as an adjunctive modality given it facilitates healing and provides long-term stability to the corneal epithelium. It can serve to replace damaged basement membrane after chelation or ablation, and protease inhibitors in the amniotic membrane may inhibit surface neovascularization.

Cross-References

- ▶ Chelation Therapy, for Calcific Band Keratopathy
- ▶ Hypercalcemia: Corneal Changes

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Calcific Keratopathy

▶ Calcific Band Keratopathy

Calcified Epithelioma of Malherbe

► Pilomatrixomas

Calcium Hydroxyapatite Deposition

► Calcific Band Keratopathy

Canaliculitis

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Synonyms

Chronic conjunctivitis

Definition

Canaliculitis is a disease characterized by inflammation of the proximal lacrimal draining system (Fulmer et al. 1999). It is often chronic and caused by infection of the lacrimal canaliculi. It is often misdiagnosed as conjunctivitis (Fulmer et al. 1999).

Etiology

The most common cause of canaliculitis is infection, but it can also be caused by a complication of punctal or intracanalicular plug insertion or intubation (Fulmer et al. 1999). The most common pathogens that cause infection include *Staphylococcus* spp., *Streptococcus* spp., *Actinomyces* spp., and *Propionibacterium* spp. (Freedman et al. 2011). The infection will often cause small concretions that consist of sulfur granules, and these can form pockets where the antimicrobial property of tears cannot reach (Freedman et al. 2011).

Clinical Presentation

Patients with canaliculitis will typically present with epiphora, lower eyelid erythema, medial canthal swelling, and recurrent conjunctivitis (Freedman et al. 2011). There is often the presence of what is known as pouting punctum, where the punctum is erythematous and raised. The pouting punctum can also be associated with mucopurulent discharge (Kanski and Bowling 2011). The involved area is often tender to touch (Kanski and Bowling 2011). Patients often have a history of unilateral conjunctival inflammation and discharge that persisted despite the use of antibiotic drops (Freedman et al. 2011).

Diagnosis

The diagnosis of canaliculitis can be made clinically. Pressure over the punctum that leads to purulent discharge can be useful in confirming the diagnosis. However, canaliculitis is often misdiagnosed due to its coincidental symptomatology with other eye disorders (Freedman et al. 2011). Objective tests for canaliculitis with an infectious etiology include those that attempt to determine the causative organism. Swabbing and needles are used to obtain samples for staining and culture. Histopathological examination including gram, periodic acid-Schiff, and Grocott's methenamine silver staining is helpful in determining the causative organism (Freedman et al. 2011). More recently, ultrasound is being used to confirm diagnosis (Freedman et al. 2011).

Differential Diagnosis

The differential diagnosis includes:

- Chronic conjunctivitis
- Dacryocystitis
- Obstruction of nasolacrimal duct
- Carcinoma of the lacrimal canaliculus

Prophylaxis

None is indicated for canaliculitis.

Therapy

Medical Management

Medical management of canaliculitis is rarely curative (Freedman et al. 2011). However, topical and systemic antibiotics have been shown to improve symptoms. Systemic use of penicillin and topical neomycin, polymyxin, or bacitracin has all been shown to help symptoms. The failure for antibiotics to be curative is thought to be due to the inability of antibiotics to penetrate canalicular concretions. Warm compresses and digital massage are other techniques that are utilized.

Surgical Management

Surgical management is the definitive treatment for canaliculitis (Freedman et al. 2011). Canaliculotomy is the procedure most commonly utilized to cure canaliculitis. In a canaliculotomy, a probe is passed through the canaliculus in order to open it. Then the concretions are extracted using a curette. An antibiotic solution is then added to the canaliculus. Risks to the procedure include canalicular scarring, lacrimal pump dysfunction, and failure to treat concretions that are deeper in the canaliculus.

Prognosis

The prognosis of the patient's illness is likely to depend on the duration of the disease prior to diagnosis, the treatment employed to manage the disease, comorbidities, and other less understood variables (Freedman et al. 2011). After treatment with canaliculotomy, continued symptoms have been shown to occur in 27% of patients (Zaldivar and Bradley 2009).

Epidemiology

Canaliculitis is a relatively rare disorder, but it is also generally underreported and frequently misdiagnosed (Freedman et al. 2011). It is most common in patients over the age of 50. There is a high female/male ratio, and there does not seem to be any racial or ethnic association (Freedman et al. 2011).

Cross-References

▶ Conjunctivitis
▶ Dacryocystitis

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Cancer, Retinopathy Associated with

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Synonyms

Cancer-associated retinopathy; CAR

Definition

Paraneoplastic syndrome is a complex of signs and symptoms mediated by hormones or immune

response among cancer patients. It is estimated to occur in as many as 10% of cancer patients (Retina and Vitreous 2014–2015).

Paraneoplastic syndromes involving the visual system are rare and estimated to affect as little as 0.01% of patients. One of the main two visual paraneoplastic syndromes is cancer-associated retinopathy (CAR), which can cause retinal degeneration by immunologic mechanism.

The most common malignancies which are associated with CAR include: small-cell lung carcinoma, ovarian cancer, endometrial and cervical cancer, and breast cancer. In rare cases CAR may be associated with non-small-cell lung cancer, lymphoma, other hematological malignancies, and bladder carcinoma (Rahimy and Sarraf 2013).

The mean age of CAR symptoms onset is 65 years. It is more common in women and recently reported to be 2:1 female-to-male ratio. Visual loss is painless, develops over weeks to months, and precedes the diagnosis of underlying malignancy in nearly half of patients.

Molecular mimicry has been proposed as the pathogenic mechanism behind the disease. It is hypothesized that the cancerous tumors express protein antigens that are similar or can cross-react with retinal proteins. The two most common and specific retinal proteins shown to be the target of the antigenic cross-reactivity in CAR patients are the 23-kDa retinal antigen (recoverin) and the 46-kDa antigen (a-enolase). Other retinal proteins which have been found to be antigenic include: arrestin, transducin, and neurofilament protein.

Both rods and cones are affected. Symptoms include photosensitivity, photopsias, glare, severely reduced central vision, and impaired color perception. Rod dysfunction may present as nyctalopia, impaired dark adaptation, ring scotoma, or other peripheral visual field loss (Rahimy and Sarraf 2013).

Patients with CAR involving anti-recoverin antibodies typically experience a more rapidly progressive loss of vision, often prior to the cancer diagnosis. In contrast, patients with anti-enolase are characterized predominantly by cone dysfunction, with slow progression of central vision loss, often among patients with prior diagnosed malignancy (Rahimy and Sarraf 2013).

Fundus examination in CAR varies from unremarkable to findings of optic nerve pallor, arterial narrowing, and retinal pigment epithelial (RPE) thinning and mottling. A subtle vitritis may be present, as there may also be retinal vasculitis with or without cystoid macular edema (CME).

Goldmann visual field examinations document dramatic loss of visual field over a few months, and the ERG signal is severely reduced for a and b waves. Fluorescein angiography (FA) is unremarkable in the vast majority of CAR patients, and optical coherence tomography (OCT) typically reveals severe macular atrophy, often associated with thinning of the photoreceptor layer, disruption or loss of the inner segment/outer segment (IS/OS) junction, and loss of the inner highly reflective layer.

Although no effective treatment for CAR exists, immunosuppressive therapy given in close cooperation with the patient's oncologist may halt and sometimes reverse the vision loss in patients with CAR. A combination of systemic corticosteroids, plasmapheresis, and intravenous immunoglobulin (IVIg) that presumably decrease circulating autoantibody titers and their resultant destruction of photoreceptors might be beneficial in some cases (Rahimy and Sarraf 2013; Retina and Vitreous 2014–2015).

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Cancer-Associated Retinopathy

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Synonyms

Autoimmune retinopathies; Cancer-associated retinopathy (CAR); Paraneoplastic retinopathy; Recoverin-associated retinopathy (RAR)

Definition

Cancer-associated retinopathy (CAR) belongs to a spectrum of uncommon autoimmune disorder in which autoantibodies are directed against various retinal components and can lead to progressive vision loss.

Etiology

There are many antibodies that have been discovered directed against specific retinal proteins (e.g., recoverin (23-kD retinal protein), anti-enolase, anti-arrestin, transducin B, TULP1, heat shock protein (HSC 70), carbonic anhydrase, and other antibodies to the photoreceptor cell-specific nuclear receptor (PNR) gene products). These antibodies can trigger a cascade of events, leading to increased phosphorylation of rhodopsin, which causes increased intracellular levels of calcium and activates apoptotic pathways, resulting in photoreceptor cell death. CAR usually affects both rods and cones but there are forms that preferentially or predominantly affect rod or cone function.

CAR is considered the most common form of paraneoplastic retinopathy and the most common associated malignancy is small-cell lung cancer. Multiple different malignancies however including gynecologic, breast, non-small cell lung cancer, Hodgkin lymphoma, pancreatic, prostate, bladder, laryngeal, and colon cancers have also been reported to cause CAR.

Clinical Presentation

Patients with CAR typically present with rapid, painless vision loss associated with photopsias and photosensitivity. Symptoms are usually bilateral, but occasionally occur sequentially, and then are relentlessly progressive over weeks to months. In most cases of CAR, vision loss occurs before malignancy is diagnosed. In contrast to CAR, vision loss due to melanoma-associated retinopathy (MAR) usually occurs in patients with known melanoma (often at the stage of metastasis). Symptoms and signs depend on which retinal elements are affected. Cone dysfunction causes photosensitivity, hemeralopia (day blindness or prolonged glare after light exposure), loss of central vision, and loss of color vision. On the other hand, rod dysfunction causes nyctalopia (night blindness, difficulty seeing in dim illumination), prolonged dark adaptation, and peripheral field loss. In either case, positive visual phenomena (i.e., photopsias) are often prominent, including flashing of lights, flickering, smoky, or swirling vision. At presentation the fundus findings are often normal**.** Characteristic changes occur over time however including vascular attenuation and sheathing of the retinal arterioles; thinning and mottling of the retinal pigment epithelium (RPE), vitreous cells, and periphlebitis; and eventual optic atrophy OU.

Diagnostics

There is no universal diagnostic criterion for CAR, and the diagnosis is usually made by a combination of patient's clinical symptoms, exam findings, electrophysiologic (e.g., ERG), and laboratory testing (e.g., serum paraneoplastic CAR antibodies).

The diagnostic procedures that may help in the diagnosis of CAR include visual field testing which may show central, cecocentral, or equatorial scotomas. Fluorescein angiography may be normal or might show mild peripheral vascular leakage consistent with vasculitis.

Retinal optical coherence tomography (OCT) may show thinning of the inner retinal layers.

Full-field electroretinogram (ERG) is almost always abnormal in CAR with attenuated or the absence of photopic and scotopic responses. Multifocal electroretinogram (MERG) is useful in selected cases in which visual field loss is localized centrally (e.g., paraneoplastic cone dysfunction). Laboratory testing for positive antibodies against retinal proteins is often diagnostic but may vary between laboratories. Physicians should keep a high index of suspicion based on the clinical findings, and a full work-up for an occult malignancy (e.g., PET scan) should be performed in CAR.

Differential Diagnosis

- Optic neuropathy includes compressive optic neuropathy, demyelinating optic neuropathy, ischemia optic neuropathy, toxic-nutritional optic neuropathy, and hereditary optic neuropathy.
- Retinitis pigmentosa, other hereditary or acquired retinopathies.
- Cone dystrophy.
- Acute zonal outer occult retinopathy (AZOOR).

Prophylaxis

Non-applicable

Therapy

Systemic immunosuppression medication is the mainstay of CAR therapy (e.g., steroid, cyclosporine, or azathioprine). Other immunemodulator therapies, such as intravenous immunoglobulin (IVIG), plasmapheresis, rituximab, and alemtuzumab, had been used with variable success and sometimes combinations of these treatments may be necessary.

Treatment of the underlying primary tumor is important (e.g., surgery, chemotherapy, and radiation therapy) but may not alter the visual prognosis.

Prognosis

Overall there is little to no significant visual improvement in patients with CAR despite treatment and the prognosis is generally poor.

Epidemiology

CAR is rare but the exact prevalence is unknown. It usually affects older adults, but it had been reported in younger patients too. There is no known ethnic or sex predilection.

Cross-References

- ▶ Acute Zonal Occult Outer Retinopathy (AZOOR)
- ▶ Arteritic Ischemic Optic Neuropathy
- ▶ Atypical Retinitis Pigmentosa (RP)
- ▶ Cancer, Retinopathy Associated with
- ▶ Cancer-Associated Retinopathy (CAR)
- ▶ Carbonic Anhydrase Inhibitors, for Cystoid Macular Edema
- ▶ Demyelinating Optic Neuropathy
- ▶ Inherited Cone Dysfunction
- ▶ Optic Neuropathy
- ▶ Retinopathy
- ▶ Rod-Cone Dystrophy
- ▶ Toxic/Nutritional and Hereditary Optic Neuropathy

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Cancer-Associated Retinopathy (CAR)

▶ Cancer-Associated Retinopathy

Cancer-Associated Retinopathy (CAR) Antigen

▶ Recoverin

Candida (Candidiasis), Ocular Infection/Inflammation Caused by, Endogenous Endophthalmitis

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Synonyms

Candidiasis; Candida endophthalmitis; Endogenous endophthalmitis

Definition

Candida is the most common cause of endogenous endophthalmitis. It typically affects patients who are sick, have undergone surgical procedures such as bowel surgery, and have required intravenous lines over a period of time that can result in permanent vision loss. Diagnosis is based on clinical signs and may be supported by positive fungal cultures and PCR for fungal DNA when available. Treatment includes combining systemic and intravitreal antifungal drugs, though a poor visual outcome is still a common occurrence.

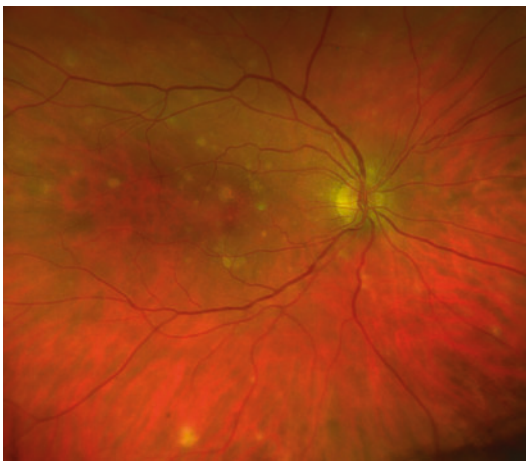
Etiology

Candida is a genus of yeasts and is the most common cause of fungal infections worldwide. Grown in the laboratory, *Candida* appears as large, round, white, or creamy colonies with a yeasty odor on agar plates at room temperature. Many species are harmless commensals or endosymbionts of hosts including humans and form part of the normal mucosal flora of the respiratory, gastrointestinal, and female genital tracts. However, when mucosal barriers are disrupted or the immune system is compromised, they can invade and cause disease. Certain factors, such as prolonged antibiotic use, increase the risk of *Candida* infection and can lead to gastrointestinal *Candida* overgrowth and penetration of the intestinal mucosa. People with uncontrolled diabetes mellitus, patients requiring intensive care, surgical patients (particularly those who have had bowel surgery), patients with a central venous catheter, very low-birth-weight infants, or those with an impaired immune system, such as those with human immunodeficiency virus infections, are more susceptible to yeast infections (Sallam et al. 2006; Das et al. 2011). While there are over 20 species of *Candida* yeasts that can cause infection in humans, *Candida albicans* is the most commonly isolated species, found in over half of cases, and can cause infections (candidiasis) in humans and other animals. Other strains that are related to human disease include *Candida tropicalis*, *Candida parapsilosis*, and *Candida*

glabrata, all of which can be involved in endogenous endophthalmitis and might have different drug sensitivities than *Candida albicans. Candida* can infect many organs and symptoms vary depending on the area of the body that is involved. Invasive candidiasis occurs when *Candida* species enter the bloodstream (candidemia) and spread throughout the body, involving vital organs such as the brain, heart, kidneys, and eyes. Endogenous *Candida* endophthalmitis is an uncommon intraocular infection that occurs as a complication of candidemia (Sallam et al. 2006).

Clinical Presentation

Following hematogenous spread the choroid is the primary site involved in ocular infection, with secondary involvement of the retina (chorioretinitis) and the vitreous, formation of multiple small vitreous abscesses and a dense suppurative vitritis. Patients typically present with subacute onset of new floaters, blurred vision, and occasionally photophobia or ocular pain. In cases where the retinal lesions are few or peripheral (Fig. 1), patients may be asymptomatic and be referred for ophthalmic examination as they are known to have systemic fungal infection.

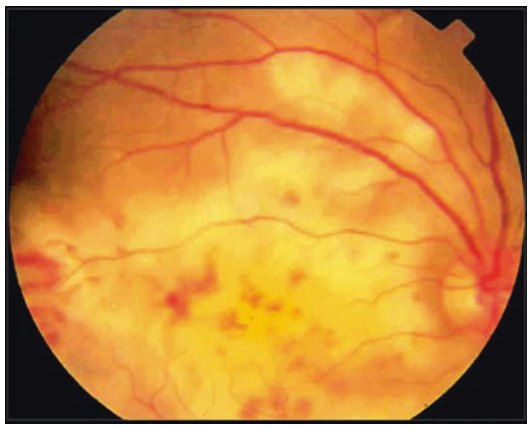


***Candida* (Candidiasis), Ocular Infection/Inflammation Caused by, Endogenous Endophthalmitis, Fig. 1** Retinal view of a patient with scattered chorioretinal lesion of *Candida albicans*

Anterior segment involvement, with or without a hypopyon or keratic precipitates, may occur. The most distinct feature of chorioretinal involvement with *Candida* is fluffy, creamy-white, chorioretinal lesions, which may be single or multiple, associated with vitreous haze (Fig. 2). Lesions may be bilateral, even when symptoms are uniocular. With extension of the lesions from the retina into the vitreous, puff ball-like vitreous abscesses may be formed. Other nonspecific lesions such as retinal hemorrhages, nerve fiber layer infarcts, and white-centered hemorrhages (Roth spots) may be seen in up to 20% of cases. Retina vessel involvement can lead to vascular occlusion, which is a poor visual prognostic factor.

Diagnosis

The diagnosis of *Candida* endophthalmitis is usually based on the appearance of typical clinical findings in patients with known systemic infection or risk factors. In cases when *Candida* endophthalmitis is suspected, the isolation of the fungus from the blood, urine, or other suspected sites can support the diagnosis. However, blood cultures may be negative in up to 50% of *Candida* endophthalmitis cases, possibly due to intermittent blood fungemia. Similarly, positive cultures from vitreous samples can have a very poor yield,



***Candida* (Candidiasis), Ocular Infection/Inflammation Caused by, Endogenous Endophthalmitis, Fig. 2** Macular involvement of *Candida albicans*

and though samples obtained by vitrectomy are more likely to be positive, over 50% of them may still be negative (Das et al. 2011). The use of polymerase chain reaction systems for detection of fungal DNA may increase the chance of identifying the causative organism and may even be able to detect *Candida* DNA through aqueous humor samples obtained from an anterior chamber paracentesis (Ogawa et al. 2012).

Differential Diagnosis

While *Candida* is the leading cause of fungal endophthalmitis and should be considered in any patient with a positive blood or urinary culture or in immunocompromised patients, bacteria remain the most common cause of endophthalmitis and vitreous samples must be examined for bacteria as well as other fungi known to be related to endogenous endophthalmitis, including *Aspergillus* and *Dimorphic* species. Acute retinal necrosis from herpetic viral infection causes extensive necrotizing retinal damage with vitritis and anterior chamber inflammation and together with toxoplasma retinochoroiditis should be considered in any case of an anterior chamber inflammation with a dense vitritis and retinitis.

Prophylaxis

Patients at high risk of developing systemic and ocular *Candida* infection should be examined repeatedly while they are at risk, as ocular infection may develop up to 2 weeks after the initial positive blood culture. In cases of patients with known candidemia, prompt use of systemic antifungal treatment can reduce the risk of developing ocular involvement. Once the patient has been identified, early ophthalmic examination should be performed or immediately in case of any ocular complaints.

Therapy

Treatment for *Candida* endophthalmitis should be instituted as soon as the diagnosis is made, and both ocular and systemic treatments should be initiated. Though there are no clear guidelines for the duration of treatment, it should be continued for at least 6–12 weeks, until all visible lesions resolve, to ensure eradication of both ocular and systemic infections. Systemic antifungal agents are effective in controlling the systemic infection as well as any choroidal involvement as the choroid is outside the blood-retinal barrier (BRB). Amphotericin B is the most commonly used agent for systemic candidiasis which is usually given as an intravenous infusion over several hours and may be given in liposomal form to reduce renal toxicity. However, when given systemically either in the soluble or liposomal form, amphotericin B does not penetrate the BRB well and does not achieve a therapeutic level within the eye. Fluconazole both orally and intravenously does cross the BRB well and achieves therapeutic levels within the eye.

While systemically administered antifungal drugs should be used in any case of *Candida* endophthalmitis to address the systemic infection, additional intravitreal therapy should also be given to achieve a high therapeutically effective intraocular level of the drug amphotericin B, which is the most widely used agent for intravitreal injections at a recommended dose of 5–10 μg in 50–100 μl. In cases of *Candida* species known to be resistant to fluconazole and amphotericin, voriconazole can be used both systemically and intravitreally.

Vitrectomy should be considered in all patients with severe vitreous involvement. This can reduce the fungal load and improve the drug effect, as well as provide further specimens for diagnosis. Most importantly, vitrectomy can also reduce the risk of retinal detachment following vitreous infection as this can occur from vitreous contraction pulling on the retina.

Prognosis

The prognosis of *Candida* endophthalmitis depends on the location of the abscesses and the extent of ocular damage before the start of effective treatment. Visual loss is commonly related to the

development of retinal detachments, fibrotic membranes, or infective lesions which involve the optic disk or macula. However, patients with candidemia and tissue invasive candidiasis can have a high mortality rate that can reach up to 50%.

Epidemiology

Candida is an uncommon cause of endogenous endophthalmitis and accounts for approximately 6% of culture-proven endophthalmitis (Schimel et al. 2013). The most common fungus is *Candida albicans* followed by the *Aspergillus* species, and endophthalmitis has been diagnosed in 2.5% of patients with known candidemia (Sallam et al. 2006).

Cross-References

- ▶ Amphotericin B, for Aspergillus Endophthalmitis
- ▶ Aspergillus (Aspergillosis), Endogenous Endophthalmitis
- ▶ Endophthalmitis

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Candida Endophthalmitis

▶ *Candida* (Candidiasis), Ocular Infection/Inflammation Caused by, Endogenous Endophthalmitis

Candida Keratitis/Ocular Infection

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Synonyms

Fungal corneal infection; Keratomycosis

Definition

Candida keratitis is a potentially sight-threatening corneal infection that most commonly develops in patients after trauma or in those with a compromised corneal surface.

Etiology

Fungi are a group of microorganism that has rigid walls and a distinct nucleus with multiple chromosomes containing both DNA and RNA. The two main types of fungi causing keratitis are:

1. Yeast (e.g., genus *Candida*), ovoid unicellular organism that reproduces by budding, is responsible for most cases of fungal keratitis in temperate climates. Yeast is a common offender in the northern and coastal regions of the United States, constituting 32–43% of the keratomycoses, and commonly occurs in the eyes with predisposing alterations in host defenses.
2. Filamentous fungi (e.g., genera *Fusarium* and *Aspergillus*), multicellular organisms that produce tubular projection known as hyphae, are the most common pathogens in tropical climates.

Fungi gain access to the corneal stroma through a defect in the epithelial barrier. Once in the stroma, they multiply and cause tissue

necrosis, leading to a host inflammatory reaction. Organisms can penetrate deep into the stroma and through an intact Descemet's membrane. It is thought that once organisms gain access to the anterior chamber, eradication of the organisms becomes extremely difficult. Likewise, fungi that extend from the cornea into the sclera become difficult to treat.

Risk Factors

1. Trauma to the cornea with plant or vegetable material is the leading risk factor for fungal keratitis.
2. Wearing contact lens is another risk factor for the development fungal keratitis.
3. Topical corticosteroids are a major risk factor as well, as they appear to activate and increase the virulence of fungal organisms by reducing the cornea's resistance to infection.
4. Candida species cause ocular infections in immunocompromised host and in corneas with chronic erosions/ulceration from other causes.
5. Other common risk factors include corneal surgery (e.g., penetrating keratoplasty) and chronic keratitis (e.g., herpes simplex virus, herpes zoster).

Clinical Presentation

Presentation is with a gradual onset of pain, grittiness, photophobia, blurred vision, and watery or mucopurulent discharge.

Signs

– Candida keratitis: yellow-white densely suppurative infiltrate and collar-stud morphology may be seen. Candida ulcers occasionally have distinct oval outlines with a plaque-like surface.
– Filamentous keratitis: gray or yellow-white stromal infiltrate with indistinct fluffy margins. Progressive infiltration often is associated with satellite lesions.
  - Feathery branch-like extension or a ring-shaped infiltrate may develop.
  - Rapid progression with necrosis and thinning can occur.
  - Penetration of an intact Descemet's membrane may occur and lead to endophthalmitis without evident perforation.
  - An epithelial defect is not invariable and is sometimes small when present.
  - Other features include anterior uveitis, hypopyon, endothelial plaque, increased intraocular pressure, scleritis, and sterile or infective endophthalmitis.

Diagnostics (Lab Diagnostics)

- History of trauma involving vegetative matter is highly suggestive.
- Lack of response to conventional antibacterial therapy.
- Corneal scraping for staining with gram, Giemsa, Gomori methenamine silver, and calcofluor-white stains.
- Cultures, media include sheep blood agar, chocolate agar, and thioglycolate broth. Initial growth occurs within 72 h in 83% of cultures and within 1 week in 97% of cultures.
- Corneal biopsy may be required if smear and cultures are negative and is indicated in the absence of clinical improvement after 3–4 days.
- Other less widely used methods for identification of fungi include electron microscopy and polymerase chain reaction.

Differential Diagnosis

Differential diagnosis includes bacterial, herpetic, and *Acanthamoeba* keratitis. It is important to be aware of coinfection, including with an additional fungal species.

Prophylaxis

The patient's chief concern should be noted, and a complete systemic and ocular history, eliciting specific risk factors for infection of the external eye, should be obtained. A detailed history and

physical examination are essential to proper diagnosis of external eye infections.

Therapy

Initially the fungal infection should be treated medically and potentially surgically, as fungal infection can be rapidly destructive to the integrity of the eye. Hospital admission may be necessary. Topical and systemic treatment usually lasts for several weeks to months. Lack of disease progression is the first therapeutic response.

Medical Therapy

- Removal of the epithelium over the lesion may enhance penetration of the antifungal agents.
- Topical treatment of the antifungal agents should initially be given hourly for 48 h and then reduced as signs permit. Because most antifungals are fungistatic, treatment should be continued for at least months.
- Candida is treated with amphotericin B 0.15% or econazole 1%; alternatives include natamycin 5%, fluconazole 2%, and clotrimazole 1%.
- Filamentous infection is treated with natamycin 5% or econazole 1%; alternatives are amphotericin B 0.15% and miconazole 1%.
- A broad-spectrum antibiotic prevents bacterial coinfection.
- Cycloplegia for comfort.
- Subconjunctival fluconazole may be used in severe cases.
- Systemic antifungals may be given in severe cases, when lesions are near the limbus, or for suspected endophthalmitis, options include oral voriconazole, itraconazole, or fluconazole 200 mg.
- Tetracycline (e.g., doxycycline) may be given for its anti-collagenase effect when there is significant thinning.
- IOP should be monitored.

Surgical Therapy

Debridement and superficial keratectomy, although mostly of diagnostic benefit, may enhance the effectiveness of medical treatment.

Conjunctival flaps have been advocated for nonhealing ulcers and are often effective. Therapeutic keratoplasty (penetrating or deep anterior lamellar) is considered when medical therapy is ineffective or following perforation or impending scleral extension.

Prognosis

The prognosis varies depending on the depth and size of the lesion and the causative organism. In general, small superficial infections respond well to topical therapy. Deep stromal infections and infections with concomitant scleral or intraocular involvement are much more difficult to eradicate.

Three factors significantly associated with treatment failure of fungal keratitis: large ulcer size (greater than 14 mm), the presence of hypopyon, and Aspergillus as causative organism.

Epidemiology

Fungi may be part of the normal external ocular flora; they have been isolated from the conjunctival sac in 3–28% of healthy eyes in various series and can be recovered from diseased eyes with greater frequency (17–37%).

Aspergillus species are the most common organism responsible for fungal keratitis worldwide. However in the United States, Candida species is the most common etiology.

Overall, the incidence of fungal keratitis is low (6–20%). More reports of fungal keratitis originate from the southern United States, and it continues to be a disease most commonly encountered in patients who come from a rural setting.

Cross-References

▶ Necrotizing Keratitis
▶ Nonnecrotizing Keratitis
▶ Peripheral Keratitis

Further Reading

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Candidiasis

► *Candida* (Candidiasis), Ocular Infection/Inflammation Caused by, Endogenous Endophthalmitis

Candle Power (Luminous Intensity)

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Definition

Candle power is a photometric measure of the quantity of light I [lm] emitted by a light source into a solid angle Ω [sr]. The unit for candle power is candela [cd] which is equal to [$lm \cdot sr^{-1}$]. Its physical definition as one of the base units in the International System of Units (SI) is the amount of light at a frequency of $540 \cdot 10^{12}$ Hz with an intensity of 1/683 $W \cdot sr^{-1}$.

Cross-References

► Frequency of Light Wave
► Luminance: Definition
► Radiance

Can-Opener Capsulotomy

► Can-Opener Technique

Can-Opener Technique

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Synonyms

Can-opener capsulotomy; Letter-box technique; Multipuncture capsulotomy

Definition

Technique of opening the anterior capsule by perforation, traditionally used in pediatric cataract surgery.

The terms describing the mentioned method derive either from the postage-stamp application technique or can-opener method.

Epidemiology

This technique has been largely superseded by the introduction of the capsulorhexis. Therefore, recent epidemiology is unknown.

History

Years after the introduction of anterior capsulotomy technique associated with intraocular lens implantation (IOL), Little and Pearce developed the multipuncture capsulotomy before Ganald and Baikhof established the envelope capsulotomy (horizontal) in 1979. Back then the can-opener technique came to common use.

Clinical Features

A bent-needle cystotome is stitched several times through the anterior capsule. Jointly punches form a circular opening.

Tests

See "► Cataract Surgery" entry.

Differential Diagnosis

Other capsular opening methods in the following are:

- Can-opener technique (letter-box technique): traditionally used in pediatric cataract surgery, for the planned extracapsular extraction, using a disposable or commercially available cystotome, several punctuations (60–80)
- Linear capsulotomy

  Capsulopuncture

Etiology

See "History" section above.

Treatment

The technique uses single stitches around the anterior capsule (60–80). After that, the edges of the anterior capsule show a jagged design which disappears shortly during retraction.

Cross-References

► Anterior Capsule Opacification (ACO)
► Continuous Curvilinear Capsulorhexis (CCC)
► Cataract Surgery

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C

Canthal Reconstruction

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Synonyms

Medial and/or Lateral canthal reconstruction

Definition

Reconstruction of the medial and/or lateral canthal structures.

Indication

Canthal reconstruction is utilized for defects arising from cancer resection surgery (including Mohs surgery), trauma, involutional changes, or congenital deformities in the medial and/or lateral canthus. The goals of canthal reconstruction include recreation of a stable canthus with adequate eyelid support while maximizing cosmesis and symmetry.

Contraindication

Patients with significant trauma to the canthal regions should be evaluated for other injuries whose repair would take precedence, such as a ruptured globe. Incisions utilized in canthal

reconstruction can result in scarring of the canthal region and possible rounding or phimosis of the canthal angle.

Techniques and Principles

Techniques for canthal reconstruction are dictated by the extent of the defect and the structures involved.

Medial canthal injuries and defects are unique in that they may involve the lacrimal outflow system. A thorough evaluation of the lacrimal outflow system is of the utmost importance in evaluating medial canthal injuries, and any coexisting injury to these structures should be repaired at the time of canthal reconstruction. Injury to the medial canthal tendon often portends canalicular system injury, which should be evaluated and repaired. Repair of an avulsed medial canthal tendon can be achieved by multiple techniques depending on the status of the surrounding boney structures. The ultimate goal is that of recreation of a normal medial canthal region with a proper posterior vector of the medial canthal tendon to allow proper eyelid support for normal function. Suturing the tendon to the periosteum of the posterior lacrimal crest is often a mainstay of treatment. However, if significant boney trauma is also present as in the case of nasoethmoidal fractures, then techniques such as mini-plating or transnasal wiring may be required for proper reconstruction. Reconstruction then addresses any loss of anterior lamellar tissue. Options are varied and depend on the defect size and position but include secondary intention healing, direct closure, local advancement flaps, and full thickness skin grafts.

The ultimate goal of lateral canthal reconstruction is recreation of a lateral canthus with adequate anterior and posterior lamellar structures and a lateral canthal angle, which has a posteriorly directed vector and appropriate tension to allow adequate eyelid support for normal function. In cases of lateral canthal defects which also include full thickness eyelid defects, appropriate tarsal/canthal tendon substitutes must be used and can include free tarsal grafts, tarsal transposition grafts including lid sharing techniques, tarsal substitutes such as hard palate or nasal septum, or local periosteal flaps. Emphasis is on recreation of a lateral canthus with appropriate tension and vector direction (posteriorly directed, hugging the contour of the globe) achieved by ensuring the canthal tendon, or its substitute, is secured to the inner aspect of the lateral orbital rim periosteum in the region of Whitnall's tubercle. In cases with extensive injury, which can include underlying boney injury as well, for example, trimalar fractures which can displace the entire lateral orbital rim, the boney fractures must be repaired to allow adequate canthal reconstruction. If adequate periosteum in the region of Whitnall's tubercle is not present to allow proper lateral canthal tendon fixation, drill holes with wiring may need to be utilized. Anterior lamellar reconstruction can be achieved by various methods; the choice is partly dependent on whether a vascularized flap is required to support posterior lamellar free grafts which may have been used in the reconstruction. Options include direct closure, local rotational flaps (such as rhomboid flaps), local advancement flaps (such as Tenzel semicircular flaps or Mustarde cheek flaps), local transposition flaps including those from the upper or lower eyelids, and full thickness skin grafts.

Outcome

The goals of canthal reconstruction include recreation of a stable canthus and eyelids with adequate eyelid support to allow maximal function, cosmesis, and symmetry.

Complications

Incisions utilized in canthal reconstruction can result in scarring of the canthal region. Failure to achieve accurate canthal vectors can result in eyelid malposition including canthal dystopia, ectropion, and entropion. Secondary rounding and phimosis

of the lateral canthal angle can occur after surgery in this region. Weakening of the orbicularis oculi muscle may occur if there is injury to the zygomatic branch of the facial nerve.

Cross-References

- ▶ Congenital Color Vision Defects
- ▶ Spasm of Eyelids
- ▶ Mustarde Flap
- ▶ Reconstructive Surgery of Eyelid
- ▶ Semicircular Flap
- ▶ Tenzel Flaps
- ▶ Transposition Flap

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Canthaxanthin, Retinopathy

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Synonyms

Tanning pills retinopathy; β, β-Carotene-4; 4′-Dione retinopathy

Definition

Canthaxanthin is one of more than 400 naturally occurring carotenoids, which is synthesized by microorganisms and plants. It is found in fruits, vegetables (chanterelle mushrooms), some crustaceans and fish. Canthaxanthin is fat-soluble and accumulates in human tissue through dietary ingestion.

Due to its red-orange hue, canthaxanthin serves as an artificial food-coloring agent. It is associated with E number E161g and is approved for use as a food coloring agent in different countries, including the USA and Europe. The safety of canthaxanthin as a feed and a food additive has been evaluated; acceptable daily intake (ADI) is of 0.03 mg/kg bodyweight.

The bronzing effect of the skin induced by oral ingestion of canthaxanthin has led to therapeutic uses in photosensitivity disorders, such as erythropoietic protoporphyria, but also to its use as an artificial tanning agent, consumed in various tanning pills. Canthaxanthin has been a popular over-the-counter oral tanning agent in Europe, Canada, and Australia since 1979. However, due to related retinopathy, its use as a tanning agent has been banned in the USA by the Food and Drug Administration.

Canthaxanthin retinopathy was first described in 1982 by Cortin et al., after ingestion of high doses of canthaxanthin consumed as tanning pills. The level of canthaxanthin intake in the affected individuals was many times greater than that which could ever be consumed via poultry products. The retinopathy was characterized by accumulation of small (30 μ) birefringent golden crystals in the retina, mainly in the perifoveal area. Fluorescein angiogram demonstrates blocked fluorescence corresponding to the perifoveal crystals.

The described incidence of canthaxanthin retinopathy is 12–14%, although the true incidence may be higher due to the relative asymptomatic course. The risk for retinopathy is dose dependent, seen in 50% of patients consuming a total dose of 37 g and in 100% of patients consuming more than 60 g. Predisposing factors proposed are age, retinal pigment epithelial (RPE) defects, central serous chorioretinopathy, ocular hypertension, retinal vein occlusion, and concomitant use of beta carotene. An extensive reduction in the

number of crystals to complete disappearance has been documented up to several years upon termination of drug consumption.

Polarization microscopy of the retina in cynomolgus monkeys, treated with high and prolonged intake of canthaxanthin, demonstrated birefringent inclusions in the inner layers of the peripheral retina and to some extent, of the central retina. Inclusions were found in the retinal nerve fiber layer, ganglion cell layer, inner plexiform layer and inner nuclear layer, and, in a lesser extent, in the outer plexiform layer (but not in the outer nuclear layer, photoreceptors or RPE). In humans, canthaxanthin deposits were found in the inner layers of the retina using light and electron microscopy. Optical coherence tomography (OCT) has demonstrated crystals in the outer plexiform layer.

Most individuals with canthaxanthin retinopathy are asymptomatic, with normal visual acuity and color perception. Prolonged dark adaptation curve and reduced retinal sensitivity in threshold static perimetry have been described. Normal electroretinography (ERG) and electrooculogram (EOG) were documented in patients with canthaxanthin retinopathy as well as normal ERG in monkeys.

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Cantholysis

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Synonyms

Canthoplasty; Inferior cantholysis; Superior cantholysis

Definition

An incision of either the inferior or superior limb of the lateral canthal tendon and lysis of the associated canthal ligamentous fibers.

Indication

Cantholysis is an integral component of multiple surgeries performed in the lateral canthal region. It is usually performed in conjunction with canthotomy. In the emergency management of orbital hemorrhage, canthotomy combined with inferior (and if needed superior) cantholysis allows decompression of the orbital compartment and hematoma evacuation. When combined with canthotomy, cantholysis allows additional horizontal eyelid mobility for closure of eyelid defects. Cantholysis is an integral step in the lateral tarsal strip operation for the management of

horizontal eyelid laxity. Inferior and/or superior cantholysis combined with canthotomy can allow improved access to the lateral anterior orbital space for orbital surgery.

Contraindication

Cantholysis, particularly when combined with horizontal shortening of the eyelid, can result in phimosis and rounding of the lateral canthus. Particularly in previously operated eyelids, weakening of the orbicularis oculi muscle may occur if there is injury to the zygomatic branch of the facial nerve.

Techniques and Principles

Cantholysis involves the incision and lysis of the inferior and/or superior canthal tendon and associated ligamentous fibers. Surgery begins with a canthotomy. Upon completion of the canthotomy, the lateral canthal tendon is composed of inferior and superior canthal tendon limbs. Cantholysis is then performed using Stevens scissors. The tendon, either inferior or superior, is strummed with the scissors and then cut close to the orbital rim. The ligamentous fibers of the canthal tendon are diffuse in their attachments to the orbital rim, and often even after lysis of the main portion of the canthal tendon, additional incision of these ligamentous fibers is needed to completely free the tendon and eyelid. Adequate cantholysis allows easy distraction of the lateral portion of the eyelid.

Outcome

At the completion of the procedure, the eyelid is freely mobile and easily distracted at the lateral canthus in all directions.

Complications

Cantholysis, particularly when combined with horizontal shortening of the eyelid, can result in phimosis and rounding of the lateral canthus, particularly in a multi-operated eyelid. Weakening of the orbicularis oculi muscle may occur if there is injury to the zygomatic branch of the facial nerve. Of particular note, in cases of emergency orbital hemorrhage management, improperly performed canthotomy and cantholysis will not allow adequate orbit decompression, hematoma evacuation, and potential vision preservation.

Cross-References

- ▶ Canthotomy
- ▶ Horizontal Eyelid Shortening
- ▶ Lateral Tarsal Strip Procedure
- ▶ Orbital Hemorrhages
- ▶ Semicircular Flap
- ▶ Tenzel Flaps

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Canthoplasty

- ▶ Canthotomy
- ▶ Cantholysis

Canthotomy

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Synonyms

Canthoplasty; Lateral canthotomy

Definition

An incision of the lateral canthal tendon.

Indications

Canthotomy is an integral component of multiple surgeries performed in the lateral canthal region. It is usually performed in conjunction with either an inferior or superior cantholysis. In the emergency management of orbital hemorrhage, canthotomy combined with inferior (and if needed superior) cantholysis allows decompression of the orbital compartment and hematoma evacuation. Canthotomy, particularly when combined with cantholysis, allows horizontal eyelid mobility for closure of eyelid defects. Canthotomy is an integral first step in the lateral tarsal strip operation for the management of horizontal eyelid laxity. Canthotomy combined with inferior and/or superior cantholysis can provide access to the lateral anterior orbital space for orbital surgery.

Contraindication

A large canthotomy incision can result in scarring of the lateral canthal region and possible rounding or phimosis of the lateral canthal angle. Particularly in previously operated eyelids, weakening of the orbicularis oculi muscle may occur if there is injury to the zygomatic branch of the facial nerve.

Techniques and Principles

A scalpel or scissors are used to create a horizontal incision through the horizontal raphe at the lateral canthal angle (the lateral junction between the upper and lower eyelids). The incision is carried down to the lateral orbital rim to ensure the tendon is completely divided into inferior and superior limbs. Hemostasis is obtained with gentle cautery to the wound edges. Alternatively, some authors suggest utilizing a straight hemostat to cause a crush injury at the horizontal raphe prior creating the incision to achieve improved hemostasis.

Outcome

At the completion of the procedure, the lateral canthal tendon is divided into superior and inferior canthal tendon limbs.

Complications

A large canthotomy incision can result in scarring of the lateral canthal region and possible rounding or phimosis of the lateral canthal angle. Weakening of the orbicularis oculi muscle may occur if there is injury to the zygomatic branch of the facial nerve. Of particular note, in cases of emergency orbital hemorrhage management, inferior and/or superior cantholysis must be combined with the canthotomy to allow adequate orbit decompression and hematoma evacuation.

Cross-References

- ▶ Cantholysis
- ▶ Horizontal Eyelid Shortening
- ▶ Lateral Tarsal Strip Procedure
- ▶ Orbital Hemorrhages
- ▶ Semicircular Flap
- ▶ Tenzel Flaps

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Capillary Hemangioma

► Vascular Tumors Disease of the Conjunctiva

Capsular Bag

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Synonyms

Lens capsule

Definition

The capsular bag is the capsule of the crystalline lens. This term applies especially to the capsule after removal of its content by extracapsular cataract extraction or phacoemulsification, usually through a circular anterior opening (capsulorrhexis). In standard phacoemulsification cataract surgery an artificial intraocular lens is placed into the capsular bag.

Cross-References

► Capsulorrhexis
► Cataract, Causes and Treatment
► Cataract Surgery
► Intraocular Lens
► Lens Capsule
► Phacoemulsification and Posterior Chamber Intraocular Lens (IOL) Implantation

Capsular Bag Distension Syndrome

► Capsular Block Syndrome

Capsular Bag Opacification

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Synonyms

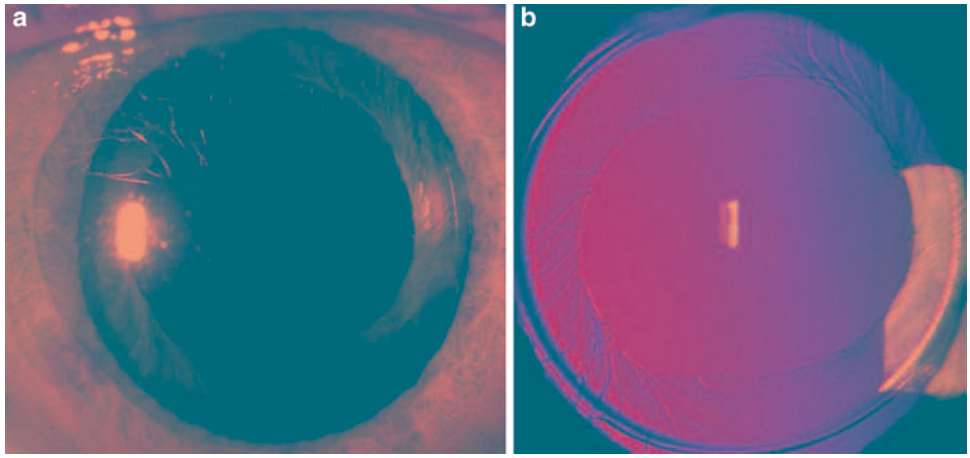
After cataract; Anterior capsule opacification (ACO); Posterior capsule opacification (PCO); Secondary cataract

Definition

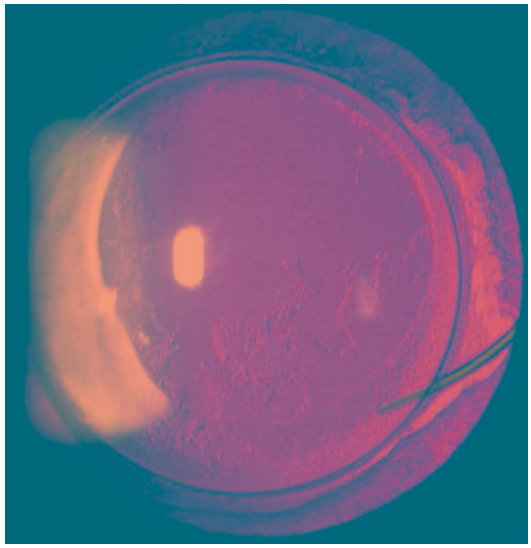
Lens epithelial cells attached to the lens capsule which have not been removed during cataract surgery (extracapsular cataract extraction) are responsible for the development of capsular bag opacifications. The surgical trauma initiates a wound-healing response provoking changes in signaling potential of lens cells that results in a promotion of proliferation rates, increased cell matrix deposition, transdifferentiation, matrix contraction, and cell differentiation (Wormstone et al. 2009) resulting in pearl formations on or whitening and shrinkage of the capsule (Menapace 2005).

Histology

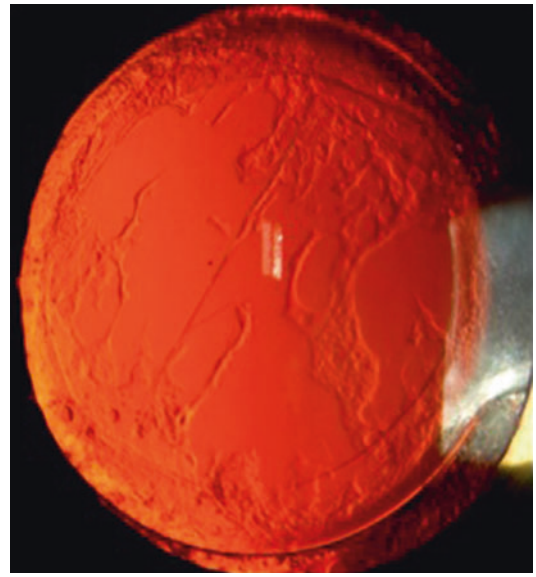
There are two different kinds of lens epithelial cells. The so-called E-cells can be found at the lens equator. These cells are very active in terms of mitosis, proliferation, and migration along the posterior capsule. The E-cells form the Elschnig's pearl or honey comb pattern of regeneratory posterior capsule opacification (PCO) which can lead to a significant reduction of visual acuity postoperatively (Apple et al. 1992; Pandey et al. 2004). It is considered a long-term complication after extracapsular cataract extraction as it becomes significant predominantly years after surgery.



Capsular Bag Opacification, Fig. 1 Slit-lamp image of an intraocular lens with beginning anterior capsule opacification (**a**) and corresponding retroilluminated image with clear posterior capsule (**b**)

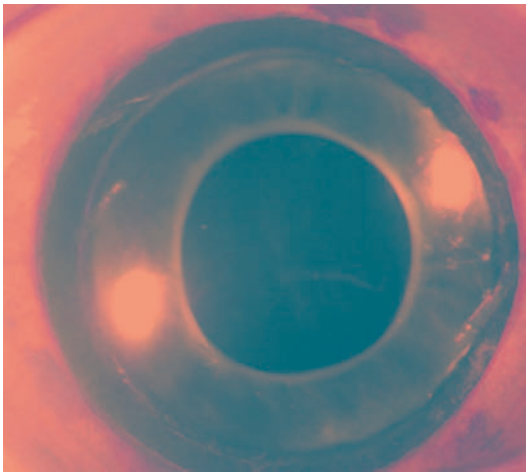


Capsular Bag Opacification, Fig. 2 Retroilluminated image: mild to moderate posterior capsule opacification

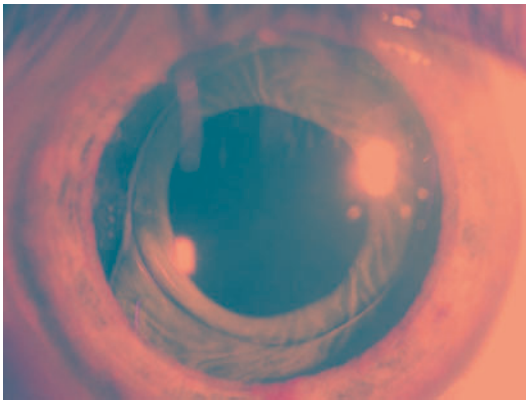


Capsular Bag Opacification, Fig. 3 Retroilluminated image: moderate posterior capsule opacification

Anterior capsule opacification (ACO), in contrast, derives from the anterior lens epithelial cells (A-cells) that cause fibrotic changes of the anterior capsule which can lead to shrinkage and whitening of the capsule (Menapace 2005). The A-cells differentiate into spindle-shaped, fibroblast-like cells and become highly contractile (Boulton and Saxby 2004). It can already be seen 3 to 6 months after surgery thus much earlier compared to PCO. Rhexis phimosis (capsule contraction syndrome) is defined as significant capsule contraction due to excessive fibrosis and can lead to secondary intraocular lens decentration (Menapace 2005). Some of these fibroblastic cells tend to migrate onto the posterior capsule as well as where they secrete



Capsular Bag Opacification, Fig. 4 Slit-lamp image: moderate anterior capsule opacification



Capsular Bag Opacification, Fig. 5 Slit-lamp image: severe anterior capsule opacification and beginning IOL decentration

extracellular matrix components leading to fine folds and wrinkling (Boulton and Saxby 2004) (Figs. 1, 2, 3, 4, and 5).

Cross-References

- ▶ Capsular Bend
- ▶ Cataract Surgery
- ▶ Intraocular Lens
- ▶ Lens Epithelial Cells
- ▶ Neodymium:YAG Laser
- ▶ Sealed Capsule Irrigation Device

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C

Capsular Bend

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Definition

Posterior capsule distension around the intraocular lens optic rim and fusion of the anterior and posterior capsule leaves within days to weeks after extracapsular cataract extraction through the production of fibrous tissue (Boulton and Saxby 2004).

Clinical Features

The capsular bending is effective in preventing posterior capsule opacification. The barrier effect is attributed to the mechanical pressure and/or the contact inhibition caused by the capsular bend (Menapace 2005). Residual fibers and epithelial cells are trapped in the space between anterior and posterior capsule. Due to continuous proliferation of lens epithelial cells and differentiation into

lens fibers in this sealed area, a Soemmering's ring formation is possible in the periphery (Boulton and Saxby 2004).

Maximal contact between intraocular lens optic and posterior capsule as well as a complete overlapping of the anterior capsule and the optic seem to be important factors for the bend formation (Menapace 2005). Its speed mainly depends on the intraocular lens design. Experimental studies of Nishi and coauthors showed the importance of the sharp optic edge design in terms of capsular bend formation regardless of the material. The authors concluded that the sharper the truncated optic edge, the sharper the capsular bend and the greater the preventive effect. Nishi et al. introduced the concept of the capsular bend index to quantify the time needed for fusion of the capsular leaves. Compared to hydrophobic and silicone IOL material, polymethyl methacrylate (PMMA) intraocular lenses showed a significant delay in capsular bend formation (Nishi et al. 2002, 2004).

Cross-References

- ▶ Capsular Bag Opacification
- ▶ Cataract Surgery
- ▶ Intraocular Lens
- ▶ Lens Epithelial Cells
- ▶ Sealed Capsule Irrigation Device

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Capsular Block Syndrome

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Synonyms

Capsular bag distension syndrome

Definition

Capsular block syndrome (CBS) first described by Davison in 1989 is defined by a postoperative or intraoperative complication after continuous curvilinear capsulorhexis (CCC) with accumulation of fluid (Viscoelasticum Healon5) between the capsular bag and the intraocular lens. A classification of Miyake et al. divides the CBS into intraoperative, early-postoperative, and late postoperative appearance.

Etiology

The groups of the classification by Miyake et al. differ according to their pathogenesis, but they all show the same aspect of an accumulated liquefied substance within a closed chamber. The mentioned substance emerges when the nucleus of the intraocular lens or its optic occludes the anterior capsule opening created by the CCC method.

An intraoperative CBS may result from the shift of capsulorhexis due to the precedently moved nucleus by hydrodissection.

In case of an early-postoperative CBS, a transparent fluid is occurring on the capsule bag, which composes a closed chamber.

The late-postoperative CBS describes the accumulation of proteins produced by remaining lenticular epithelial cells; therefore, the content of capsule bag is milky and fuzzy.

Clinical Presentation

Poor vision by an unexpected overrefractive myopia caused by the anterior IOL movement with a flattening anterior chamber is the main symptom.

Following clinical features include anterior optic displacement, iris diaphragm, anterior chamber flattening, an increasing distance between the posterior capsule and the implant, and accordingly adherence of the anterior capsule to the implant. A persistent uveitis was occasionally described.

Diagnostics

Diagnostic instruments to detect the locked fluid or rather the distance between posterior capsule and intraocular lens are at first primarily the slit lamp or the Scheimpflug camera. A continuative method is the examination with ultrasound or biomicroscopy.

Differential Diagnosis

Differential diagnosis should be considered a secondary cataract, an over- or under-correction, and corneal surface problem.

Also the patients may be mistakenly diagnosed with pupil block glaucoma or endophthalmitis.

Prophylaxis

An efficient intraoperative elimination of viscoelastic material and lens particulates also behind the IOL is important to prevent capsular block syndrome.

An untreated eye may develop glaucoma, posterior synechiae, or posterior capsule opacification with debris in the capsular bag.

Therapy

The main treating principle is to drain the locked fluid by performing a posterior capsulotomy, for example, with the neodymium:YAG (Nd:YAG) laser. Another form of treatment is the intraoperative aspiration of viscoelastic fluid behind the IOL.

Prognosis

The visual prognosis after appropriate treatment is good in the absence of other eye diseases.

Cross-References

- ▶ Continuous Curvilinear Capsulorhexis (CCC)
- ▶ Capsulotomy
- ▶ Cataract Surgery
- ▶ Intraocular Lens
- ▶ Neodymium:YAG Laser
- ▶ Secondary Cataract

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Capsular Tension Ring

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Definition

An intraocular implant which allows the support of the capsular bag, maintaining its original contour. The application area comprehends, for example, zonulysis (zonular dehiscence,

generalized zonular weakness), lens subluxation, prophylaxis of lens decentration, pseudoexfoliation, sector kolobomas, aniridia, alleviation of primary posterior capsulorhexis, sulcus suture fixation, and combined cataract and vitreous surgery.

Epidemiology

The idea dates back to Hara et al. in 1991. They presented a closed and flexible ring consisted of silicone, which was not only to stop migration of lens epithelial cells (LEC) but also to antagonize the postoperative deformation of capsular bag.

At about the same time, the capsular tension ring was developed by Legler and Witschel and accordingly Nagamato and Bissen-Miyajima to reduce the contraction and to maintain the circular contour of capsule bag.

This open ring was made of rigid polymethyl methacrylate (PMMA).

Finally Legler et al. reported the first implantation of a capsular tension ring in the human eyes.

Clinical Features

All commercial available implants consist of polymethyl methacrylate and present an oval configuration with two bails on rings end. The caliber of comprimed ring is between 12.5 and 10 mm.

There are modifications of the original capsular tension ring like sulcus suture ring, capsular tension segment, capsular bending rings, and foldable closed ring.

CTRs can be inserted both bimanually, using a forceps and a Y-spatula, or with appropriate injectors.

Tests

Thorough examination of the eyes and workup of the patient's anamnesis is mandatory to rule out several exclusion criteria for cataract surgery or treatment of an after cataract.

Differential Diagnosis

Other implants that are used for indications named above are as follows:

- Sulcus suture rings (Cionni)
- Capsular tension segment (Ahmed)
- Capsular bending rings (Nishi-Menapace)
- Foldable closed ring (Dick)

Etiology

See History section above.

Treatment

A capsular tension ring should be implanted into the evacuated capsular bag following meticulous cleaning. Inserting the ring implant before phacoemulsification induces increased capsular torque and impedes aspiration of cortex fibers.

The use of an injector is more convenient; bimanual implantation minimizes capsular deformation and zonular stress and the risk of capsular entanglement.

Cross-References

- ▶ Aniridia, Traumatic
- ▶ Anterior Capsulorhexis
- ▶ Cataract Surgery
- ▶ Ectopia Lentis
- ▶ Posterior Capsulorhexis

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Capsule-Type Drug Delivery System

► Ocusert Delivery System

Capsulopalpebral Fascia

► Retractors, Lower Eyelid

Capsulorrhexis

► Anterior Capsulorhexis

Capsulotomy

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Synonyms

Cystotomy; Nd:Yag-Capsulotomy

Definition

A procedure in cataract surgery or posterior capsular opacification treatment to open the anterior or the posterior portion of the lens capsule.

Epidemiology

See entry "► Cataract Surgery."

History

See entry "► Cataract Surgery."

Clinical Features

According to the method a cystitome, an Nd:YAG laser (neodymium-yttrium-aluminum-garnet) or an vitrector is used.

Tests

Thorough examination of the eyes and workup of the patient's anamnesis is mandatory to rule out several exclusion criteria for cataract surgery or treatment of an after cataract.

Differential Diagnosis

See "Cross-References" section bottom.

Etiology

See "History" section above.

Treatment

The major performed anterior capsulotomy technique today is the continuous curvilinear capsulotomy (CCC) in phacoemulsification surgery. The major performed posterior capsulotomy procedure uses an Nd:Yag laser to clear and disrupt the central portion of the opacified posterior lens capsule.

Cross-References

► After Cataract
► Anterior Capsulotomy Techniques
► Cataract Surgery
► Continuous Curvilinear Capsulorhexis (CCC)
► Nd:YAG Laser

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CAR

► Cancer, Retinopathy Associated with

Carbon Dioxide Laser

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Synonyms

CO_2 laser

Definition

A laser system with a gas discharge as active medium usually containing a mixture of CO_2, N_2, H_2, and He. Unlike the excimer laser, the physical principle is based upon emission stimulated by vibrational motion of the CO_2 molecules. CO_2 lasers emit infrared radiation at a wavelength of 10.6 μm which is absorbed by water or glass. Their application in ophthalmology is bloodless tissue surgery such as blepharoplasty.

Cross-References

► Excimer Lasers

Carbonic Anhydrase Inhibitors, for Cystoid Macular Edema

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Cystoid Macular Edema

Cystoid macular edema (CME) is retinal thickening of the macula due to disruption of the blood-retinal barrier. Leakage causes accumulation of fluid in the retina, first intracellularly and later in the extracellular spaces leading to a distortion of photoreceptor architecture and decreased vision.

Carbonic Anhydrase Inhibitors

The primary pharmacologic effects of carbonic anhydrase inhibitors (CAIs) occur through the reversible, noncompetitive binding of the drug with the carbonic anhydrase (CA) enzyme. CA catalyzes the conversion of carbon dioxide and water to bicarbonate and protons and vice versa. There are two methods of CAI administration: systemic administration (acetazolamide and methazolamide) and topical administration (dorzolamide and brinzolamide).

Mechanism of Action

The mechanism by which CAIs reduce macular edema is not completely clear. Biologically plausible mechanisms with some experimental support include:

- **Promoting retinal adhesion** – CAIs decrease blood-retinal barrier leakage and stimulate the transport of small molecules such as fluorescein across the blood-retinal barrier.

- **Subretinal fluid absorption** – CAIs stimulate ion and water transport from the retina to the choroid. Animal studies have shown that CAIs increase the absorption of surgically induced subretinal blebs.
- **Subretinal PH changes** – CAIs decrease the pH in the subretinal space. The acidification induces changes in ion and fluid transport leading to a decrease in subretinal fluid (Joussen and Wolgensberger 2012; Salvatore et al. 2013).

Clinical Indications

The treatment response to CAIs seems better when the CME is caused by diffuse injury to the blood-retinal barrier along the retinal pigment epithelium (Wolfensberger 1999). The response of retinal edema to CAIs seems less promising when the damage to the blood-brain barrier is along the retinal vessels as occurs in diseases such as diabetes or retinal vein occlusions.

Clinical evidence supports the role of CAIs as a potential treatment option for CME associated with retinitis pigmentosa and chronic uveitis. Evidence for the use of CAIs for other indications is inconclusive as the present time.

Retinitis pigmentosa (RP) – RP is a clinically and genetically heterogenous group of hereditary retinal disease resulting in a progressive loss of photoreceptors and RPE cells, which leads to impaired night vision and gradual loss of visual fields. The reported prevalence of CME in RP patients varies between 10% and 40% of cases (Salvatore et al. 2013).

Oral CAIs: Multiple studies have shown improvement in vision and decreased retinal thickness with systemic administration of acetazolamide. The most common dose used in these trials is 250 mg twice daily (Rothova 2002).

Topical CAIs: Administration of 2% dorzolamide ophthalmic solution twice daily has also been investigated with conflicting results. Some studies show no significant benefit, while others demonstrate vision improvements in about 20% of participants.

Small trials have also demonstrated efficacy for CAIs in treating CME associated with other hereditary retinal dystrophies including juvenile X-linked retinoschisis, enhanced S-cone syndrome, and choroideremia.

Uveitis – CME is a major cause of visual loss in chronic uveitis. Clinical studies support the effectiveness of short-term (<4 weeks) CAI treatment at doses of up to 1000 mg of acetazolamide daily. Younger patients (< age 55) may be more likely to benefit from treatment.

Studies investigating the long-term effects of low-dose oral acetazolamide are promising and suggest it can be a useful therapeutic option for chronic CME in uveitis. The effect seems better in patients with CME with quiescent uveitis than in patients with concomitant chronic active uveitis (Ossewaarde-van and Rothova 2011).

Side Effects

Significant side effects have been reported with the use of oral CAIs. These include loss of appetite, fatigue, nausea/vomiting, diarrhea, bitter taste in mouth, dizziness, and paresthesias in the arms and legs. Chronic use can also rarely encourage the development of kidney stones. These side effects are caused through the systemic inhibition of carbonic anhydrase isoenzymes. Patients receiving long-term treatment should be monitored closely. Topical CAIs have a significantly better safety profile with mainly local side effects such as eye irritation.

Summary

Carbonic anhydrase inhibitors have a role in the treatment of cystoid macular edema. Treatment success depends largely on patient selection. Patients who respond best present with macular edema caused by fluid leaking diffusely through the retinal pigment epithelium. This may be the

case in hereditary retinal dystrophies such as retinitis pigmentosa and in chronic uveitis especially with quiescent inflammation. Oral treatment is often more efficacious than eye drops but carry a greater risk of systemic side effects. Patients on oral therapy need to be closely monitored, especially with chronic use. The role of CAIs is less clear when the cystoid macular edema is caused primarily by a disorder in the retinal vasculature, such as in diabetes and retinal vein occlusions.

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Carcinoma In Situ, of Conjunctiva

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Synonyms

Dyskeratosis; Bowen's disease; Conjunctival intraepithelial neoplasia (CIN); Conjunctival squamous dysplasia; Intraepithelial epithelioma

Definition

Defined by abnormal malignant appearing epithelial cells replacing the entire conjunctival stratified squamous epithelial layer. If these malignant appearing stratified squamous epithelial cells extend through the epithelial basement membrane and invade the substantia propria of the conjunctiva, it is characterized as invasive squamous cell carcinoma.

Basic Characteristics

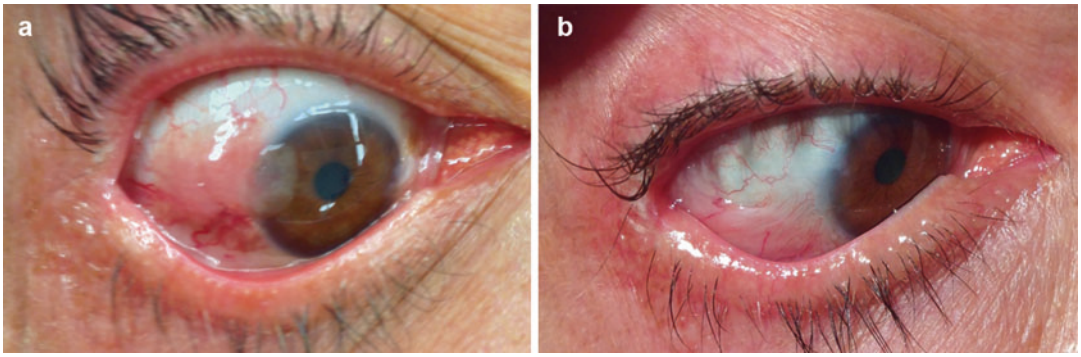
The etiology of CIN is uncertain and possibly multifactorial. The lesion most commonly develops on exposed areas of the bulbar conjunctiva, at the nasal or temporal corneoscleral limbus. Risk factors include male sex, advanced age, cigarette smoking, light complexion, prolonged sunlight exposure, and conjunctival infection by human papillomaviruses 16 and 18. In patients with AIDS, these lesions may undergo rapid growth. Immunosuppressed states seem to have a higher degree of squamous neoplasia (Lee et al. 1994).

Histology

Conjunctival tumors can range from benign hyperplastic and dysplastic lesions to malignant neoplasms. Histologically, CIN represents the presence of conjunctival epithelial dysplasia. The cells display a lack of normal organization and show an abnormal relationship to one another (polarity). In addition, cells do not mature normally as they approach the epithelial surface. If the abnormal, malignant appearing cells completely replace the conjunctival stratified squamous epithelium the term carcinoma in situ is used. If the basement membrane is penetrated, the malignant lesion is termed invasive squamous cell carcinoma.

Ocular Manifestations

Clinically these are slow-growing lesions. There are three common clinical variants. The *gelatinous* lesion consists of translucent thickening



Carcinoma In Situ, of Conjunctiva, Fig. 1 (**a**) Carcinoma in situ with visible feeder vessels and corneal overgrowth. (**b**) Two months after resection with wide margins, cryotherapy, and absolute alcohol debridement of affected cornea

that is usually not well defined. The *leukoplakic* lesion appears as a superficial white plaque pathologically representing hyperkeratosis. Only 10% will appear leukoplakic from surface keratinization. In the *papilliform* variant, a sessile papilloma contains dysplastic cells, clinically seen as a highly vascularized soft tissue mass (Erie et al. 1986). The lesions are generally located in the interpalpebral zone at the limbus. CIN or carcinoma in situ can often spread over the adjacent corneal surface (as seen in Fig. 1a and b). CIN can manifest as a pigmented tumor, resembling melanoma, due to the presence of intratumoral pigmented dendritic melanocytes. The larger the lesion, the greater the likelihood that it may be malignant. Large feeder blood vessels are also indicative of a high chance of epithelial basement membrane invasion (malignancy).

Evaluation

Given the slow growth of these lesions, patients will often be unaware of their existence. Any focal thickening of the conjunctiva, particularly when associated with prominent conjunctival vessels, should be assessed. Lissamine green and rose bengal can be used to help delineate tumor margins. Ultrasound biomicroscopy and more recently high-definition ocular coherence tomography can be used to assess scleral invasion. In any young adult, carcinoma in situ should prompt a serologic test for HIV infection.

Treatment

Suspicious lesions should be biopsied or completely excised. Excision should include 3–4 mm of surrounding benign appearing tissue. To reduce the risk of recurrence, double freeze-thaw cryotherapy to the conjunctiva adjacent to the lesion and to the scleral bed at the site of the excised limbal lesion frequently is performed. Any adjacent growth onto the cornea should be treated with absolute alcohol and removed. Greater than 90% long-term tumor control is achieved by this method (Shields et al. 2002).

Some advocates are using topical chemotherapeutic agents as a treatment or as an adjunct. Mitomycin C (0.02–0.04% solution) and 5- fluorouracil (1%) applied topically as eyedrops appear in some cases to completely eradicate CIN lesions (Shields et al. 2002). More recently, immunotherapy with interferon-a2b (0.5 mL 3 million IU/0.5 mL) has shown success with a far less toxic side effect profile (Karp et al. 2001).

Cross-References

▶ Bowen's Disease
▶ Ocular Surface Staining
▶ Squamous Cell Carcinoma of Eyelid

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Carotenes

▶ Carotenoids (Xanthophylls)

Carotenoid

▶ Beta Carotene, Use and Dosage of

Carotenoids (Xanthophylls)

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Synonyms

Carotenes; Organic pigments; Phytochemicals; Xanthophylls

Definition

Carotenoids, also known as phytochemicals, are fat-soluble plant pigments. They can be further classified as carotenes if they contain only hydrocarbons or xanthophylls if oxygen molecules are present along with the hydrocarbons (Bernstein et al. 2015). There are approximately 700 known carotenoids, while approximately 15–30 carotenoids are found in our bloodstream.

Carotenoids can absorb wavelengths from 400 to 500 nm, allowing them to absorb light energy for photosynthesis to provide protection from photo damage in plants. Carotenoids can also act as antioxidants. These include beta-carotene, alpha-carotene, beta-cryptoxanthin, and gamma-carotene. In the eye, the carotenoids which are also known as xanthophylls, lutein, and zeaxanthin are found in the macular pigment (known as the *macula lutea*). They may play important functions in the eye with their anti-oxidative capabilities and their ability to absorb damaging light from the blue and near ultraviolet spectrum.

Indication

Beta-carotene, a carotene, was tested for the prevention of lung cancer in two large NIH-supported trials in persons who were cigarette smokers or who had exposure to asbestos, both major risk factors for the development of lung cancer. Both studies showed that beta-carotene in fact increased the risk of lung cancer and mortality.

Beta-carotene was also tested in the Age-Related Eye Disease Study (AREDS) as part of a formulation of antioxidants including vitamins C and E along with zinc and copper. AREDS was originally designed as a study of the natural course and prognosis of age-related macular degeneration (AMD) and age-related cataract. The nutritional component was tested with a randomized controlled clinical trial, a 2 × 2 factorial in which the 4,757 participants were enrolled. For those with risk of AMD, they were randomized to vitamins C (500 mg) and E (400 international units), beta-carotene (15 mg) or zinc (80 mg as zinc oxide) with copper (2 mg as cupric oxide), or the combination of the vitamins and minerals. The so-called AREDS formulation was demonstrated to be beneficial for the treatment of age-related macular degeneration with a 25% reduction in the risk of having late

AMD in 5 years (Age-Related Eye Disease Study Research Group 2001).

During the course of AREDS, beta-carotene was found, as previously noted, to increase the risk of lung cancer in those enrolled in 2 NIH-supported trials of lung cancer in persons who are known to be heavy smokers or were previously exposed to asbestos. Lutein was the desired carotenoid to be studied in AREDS, but it was not commercially available when AREDS started. Observational data in AREDS also suggested that dietary lutein reduced the risk of prevalent late AMD, both neovascular and atrophic form. Thus the Age-Related Eye Disease Study 2 was initiated to evaluate the effect of adding lutein/zeaxanthin and/or omega-3 fatty acids to the AREDS formulation. Beta-carotene was found to be deleterious for former smokers in AREDS2, with a doubling of the risk of lung cancer. We have essentially replaced beta-carotene with the xanthophylls, lutein, and zeaxanthin in this formulation (Age-Related Eye Disease Study 2 Research Group 2013b). This makes biological sense as these two xanthophylls are found in the macular pigment. Both lutein and zeaxanthin are thought to be important because of their anti-oxidative capabilities and their ability to absorb damaging wavelengths of the blue and UV spectrum. Addition of lutein and zeaxanthin also resulted in an incremental beneficial effect in reducing the risk of progression to late AMD, especially the neovascular form (Age-Related Eye Disease Study 2 (AREDS2) Research Group et al. 2013a).

Indications: AREDS/AREDS2 formulations are recommended for persons with intermediate AMD (bilateral large drusen) or late AMD in one eye. Those persons with less than intermediate AMD do not benefit as these formulations do not reduce the risk of progression from early to intermediate or along the AMD scale developed from AREDS. Offsprings of those affected with AMD may be better served by having regular dilated eye exams to detect the presence of intermediate AMD. At that point, AREDS/AREDS2 formulation would be recommended.

Recently, investigators have evaluated genetic interaction with the AREDS formulation in a subgroup of AREDS participants who had genetic testing. These investigators have promoted the use of genetic testing to avoid taking zinc with specific *complement factor H* mutations. These results could not be replicated by the AREDS research team. Neither genetic testing nor avoidance of zinc in persons with intermediate AMD or late AMD in one eye is recommended. Such patients should be recommended to take the AREDS/AREDS2 formulation. Zinc alone has never been recommended as a treatment, and only the combination of antioxidant vitamins and zinc should be prescribed for those at risk. The American Academy of Ophthalmology has not recommended genetic testing for AMD, and it is not indicated prior to starting AREDS/AREDS2 formulations. Other experts in the field of genetic, epidemiology, and statistics have also weighed in with the same conclusion (Wittes and Musch 2015). Genetic testing is still reserved for research purposes.

Cross-References

- Age-Related Macular Degeneration
- Antioxidants
- Lutein
- Xanthophylls

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Carotid Cavernous Fistula

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Synonyms

Cavernous-carotid fistula; CC fistula; CCF

Definition

Carotid-cavernous fistulas (CCFs) are pathological vascular shunts where arterial blood flows directly or indirectly from the carotid artery or its branches into the cavernous sinus. CCFs can be broadly classified based on their hemodynamic characteristics, etiology, and anatomy. Hemodynamically, CCFs are divided into high-flow and low-flow fistulas. Etiologically, CCFs can be divided into spontaneous, nontraumatic and traumatic lesions. Anatomically, CCFs may be classified into direct CCFs (those that arise directly from the carotid artery) and indirect CCFs (those that arise from meningeal branches of the carotid artery). Most commonly, CCFs are divided into four types (Barrow classification).

A. Type A CCFs are direct, high-flow lesions in which the internal carotid artery (ICA) is directly connected to the cavernous sinus. Type A CCFs arise from a direct tear in the ICA wall that results from an intracavernous aneurysm rupture or trauma (including iatrogenic surgical trauma).
B. Type B CCFs are indirect, low-flow lesions arising from external carotid artery (ECA) meningeal branches.
C. Type C CCFs are also indirect, low-flow lesions but arise from ICA meningeal branches.
D. Type D CCFs are indirect, low-flow lesions arising from both ECA and ICA meningeal branches.

Etiology

A basic understanding of the cavernous sinus anatomy is required before introducing the etiologies of CCF. The cavernous sinus is a trabeculated venous cavity invested by the dura mater located lateral to the sella turcica. The cavernous sinus contains several vascular and neural structures including the ICA and multiple cranial nerves (CN) III, IV, V1, V2, and VI as well as the ocular sympathetic innervation (producing a Horner syndrome). CN VI (i.e., abducens nerve) runs lateral to the ICA and medial to the dural wall but within the substance of the cavernous sinus while the rest of the CNs (II, IV, V1, and V2) course in the lateral wall of the cavernous sinus between the two dural layers.

The cavernous sinus normally receives drainage from the superficial Sylvian vein, the superior

and inferior ophthalmic veins, and the sphenoparietal sinus. Laterally, the middle meningeal vein drains into the cavernous sinus. The cavernous sinus then drains posteriorly via the superior and inferior petrosal sinuses to the internal jugular vein. Anastomoses connecting the two cavernous sinuses include a basilar plexus of veins and an intercavernous sinus (Moore et al. 2010).

Etiologically, CCFs can be divided into traumatic and spontaneous types.

I. Traumatic CCFs

Traumatic CCFs account for up to 75% of all CCFs and they are the most common type (Type A CCF). Traumatic CCFs are most commonly seen in young male patients due to the male predominance in trauma. Traumatic CCFs can result from craniocerebral trauma and closed head injury-associated basilar skull fracture. However, they could also be a seen in projectile, perforating, or penetrating intracranial injuries. The traumatic bony fracture or shear forces can directly tear the internal carotid artery. Alternatively, a sudden increase in ICA intraluminal pressure and a concurrent distal artery compression lead to vessel wall rupture, resulting in a high-flow communication with the cavernous sinus.

II. Spontaneous CCFs

Spontaneous CCFs account for up to 30% of all CCFs in some series. In contrast to traumatic (direct, high flow) CCFs, spontaneous CCFs are typically found in older female patients, although patients of any gender and age can be affected by spontaneous CCFs. A common source of spontaneous, nontraumatic, high flow, direct CCF is a ruptured cavernous ICA aneurysm. Additionally, many genetic conditions with arterial wall defects predispose patients to spontaneous CCFs, including fibromuscular dysplasia, Ehlers-Danlos syndrome, and pseudoxanthoma elasticum. It is also proposed that microscopic venous thrombosis or increased venous pressure could cause microscopic breaks in dural vessels in the sinus and facilitate fistula formation.

Clinical Presentation

The clinical presentation of direct CCFs is caused by the pooling of highly pressurized arterial blood into the cavernous sinus, leading to venous hypertension. Direct CCFs usually have an acute and dramatic clinical presentation. The classic triad of symptoms consists of exophthalmos; cephalic or orbital bruit; and conjunctival congestion, congestion, and arterialization of vessels. Patients often complain of visual disturbances, most commonly diplopia, blurry vision, and orbital pain. Ophthalmoplegia and other cranial nerve deficits are also commonly seen in these patients. Some patients may experience facial weakness and/or facial pain. Elevated orbital venous pressure, iris and choroid congestion, and forward displacement of iris-lens diaphragm also may lead to angle-closure glaucoma. In some cases, chronic ischemia may produce neovascular glaucoma. Ophthalmoscopic findings might include venous stasis retinopathy with intraretinal hemorrhages, central retinal vein occlusion, proliferative retinopathy, retinal detachment, vitreous hemorrhage, choroidal folds, choroidal effusions, choroidal detachment, or optic disc swelling. The progression of direct CCFs is rapid and patients require urgent treatment.

In contrast, the clinical presentation of indirect CCFs is more insidious and less obvious. Indirect CCFs may not have the complete classic triad of symptoms associated with direct CCFs, and the exact pattern of symptoms depends on the characteristics of the indirect CCF, including the rate of flow, the pressure within the sinus, the location of venous drainage, and the size of the fistula. It is important to note that venous drainage patterns often change with development and resolution of thrombosis.

Anterior draining CCFs drain anteriorly into the orbit via the inferior and superior ophthalmic veins. They are the most common type of indirect CCFs and have similar but less severe symptoms than those of direct Type A CCFs. Patients with anterior draining CCFs usually present with ocular and orbital symptoms (e.g., chemosis, conjunctival injection, ophthalmoplegia, and proptosis). Diplopia may also be present if cranial

nerves or extraocular muscles are involved. A loss of vision may be present from increased intraocular pressure due to orbital venous congestion resulting in glaucoma, venous retinopathy, and ischemic optic neuropathy. However, there is often no objective or subjective bruit, and in the mildest cases there is redness of one or rarely both eyes from arterialization and dilation of conjunctival and episcleral veins. The dilated vessels have a typical tortuous corkscrew appearance of arterialization of the conjunctival/epsicleral vessels that distinguishes indirect CCFs from other diagnoses such as conjunctivitis.

Indirect CCFs that drain posteriorly into the superior and inferior petrosal sinuses may be asymptomatic. Most cases do not have any signs of orbital congestion (i.e., "white eyed shunt"), but in some cases the fistula may produce any combination of ocular motor cranial neuropathy. Patients who have ocular motor nerve paresis caused by posteriorly draining indirect CCF usually only have one affected ocular motor nerve, most commonly the oculomotor nerve (CN III). In most cases, the presentation of paresis is associated with ipsilateral orbital or ocular pain. Furthermore, some cases of posteriorly draining CCFs can cause brainstem congestion and lead to neurologic deficits.

Diagnosis

Cerebral angiography is the gold-standard imaging modality to diagnose CCFs, but patients typically undergo cranial and orbital contrast CT and MRI first. For both direct and indirect CCFs, CT and MRI findings include proptosis, enlargement of the extraocular muscles, enlargement and tortuosity of the superior ophthalmic vein, and enlargement of the ipsilateral cavernous sinus. CT and MRI studies may show dilatation of leptomeningeal and cortical veins in patients with high-flow fistula and retrograde cortical venous reflux. Furthermore, cerebral edema or hemorrhage may be seen in patients with cerebral venous congestion.

Confirmation of the diagnosis of CCF, however, is established by catheter cerebral angiography. Cerebral angiography is also crucial in classifying the CCF, delineating the patterns of venous drainage (including possible cortical venous drainage), and planning the optimal treatment (typically endovascular occlusion). Four-vessel cerebral angiography is done using transfemoral arterial catheterization with imaging of bilateral common carotid arteries (CCAs), ICAs, ECAs, and vertebral arteries.

Differential Diagnosis

1. Chronic conjunctivitis
2. Blepharoconjunctivitis
3. Dysthyroid orbitopathy
4. Orbital inflammatory pseudotumor
5. Orbital cellulitis
6. Episcleritis
7. Sphenoorbital meningioma
8. Tolosa-Hunt syndrome
9. Cavernous sinus thrombosis

Therapy

I. Direct CCF Treatment

The goal of treating direct CCFs is to occlude the fistula while preserving ICA patency if possible. Specific types of treatment will depend on the anatomy of the fistula and the clinician preference. The following are available therapies for direct CCF:

1. Transarterial embolization consists of advancing a catheter and microcatheter in the cervical carotid artery to the cavernous segment of the ICA. Embolic agents include detachable platinum coils, as well as liquid embolic agents such as n-butyl cyanoacrylate (*n*-BCA). Onyx or combinations of these agents can be used to occlude the fistula.
2. Transvenous embolization involves assessing the cavernous sinus from the venous end, such as via the inferior petrosal sinus or superior ophthalmic vein. Once at the site of fistula, detachable platinum coils or liquid embolic agents are used to occlude the site of fistula.

3. Porous stents and coils may be used alone or in combination with other embolization materials to treat large arterial tears. Self-expanding stents can also be used to reconstruct the injured ICA that caused the direct CCF.
4. Covered stents can also be used to obliterate direct CCFs by acting as an impermeable barrier across the fistula while preserving ICA patency.
5. Surgical arterial sacrifices are done for direct CCFs caused by extensive ICA injury not amenable to endovascular occlusion. It is possible that the arterial segment with the fistula might need to be occluded distally and proximally.

II. Indirect ICF Treatment

The treatment goal of indirect CCFs is to decrease the pressure in the cavernous sinus by occluding the fistulous communications. The following are treatment options for indirect CCF:

1. Carotid self-compressions are manual compression of the carotid artery about four to six times per hour for a period of 10 s each. It is particularly effective in patients with low flow fistulas in the anterior cavernous sinus and in patients with short duration of symptoms and low intraocular pressures. Contraindications include patients with declining visual function, high intraocular pressure, intolerable periocular pain, hypertensive carotid sinus syndrome, atherosclerosis stenosis, ulceration of the cervical artery, and history of cerebral ischemia. It is advised to use the contralateral hand so that if ipsilateral cerebral ischemia were to occur from compression of the ICA then the resulting hemiparesis would allow the compressing hand to fall away from the ICA.
2. Transarterial embolization is a good treatment option for indirect CCFs, but distal access into tiny feeder vessels is often difficult and may require multiple sessions.
3. Transvenous embolization is becoming the preferred treatment of indirect CCFs, and the superior ophthalmic vein can be sometimes directly accessed to treat the CCF.

Prognosis

With complete endovascular or other closure of CCF, symptoms such as chemosis and proptosis typically resolve within hours to days, while cranial nerve palsies will resolve over the course of weeks to months. Vision recovery depends on the pathogenesis, severity, and duration of deficits before intervention. Patients who suffer visual loss due to choroidal effusion or choroidal detachment may have recovery of visual function, while patients with visual loss caused by retinal or optic nerve damage may have persistence of their visual loss (Miller 2012). Recurrences of CCFs are uncommon postembolization but could be treated with repeat embolization (Ellis et al. 2012).

Cross-References

- ▶ Dural Sinus Thrombosis
- ▶ Graves' Ophthalmopathy
- ▶ Pseudotumor Cerebri

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Carpenter Syndrome

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Synonyms

Acrocephalopolysyndactyly type II; Carpenter's syndrome

Definition

Carpenter syndrome is a congenital disorder classically characterized by variable syndactyly and polydactyly (particularly preaxial polydactyly of the toes), obesity, and variable craniosynostosis (Gorlin et al. 2001).

Etiology

Carpenter syndrome is a rare, autosomal recessive disorder caused by a homozygous mutation in the RAB23 gene on chromosome 6p11. The Rab23 protein regulates the Hedgehog signaling pathway, and several key features of Carpenter syndrome such as polysyndactyly and brachydactyly are seen in other disorders associated with defective Hedgehog pathway signaling. Craniosynostosis, obesity, and other abnormalities associated with Carpenter syndrome have not shown to be implicated in the Hedgehog pathway, but further research is needed (Jenkins et al. 2007).

Clinical Presentation

Even within families, manifestations of the syndrome are highly variable.

Craniosynostosis and Central Nervous System

Carpenter syndrome patients typically present with craniosynostosis of the metopic, lambdoid, coronal, or sagittal sutures, along with possible acrocephaly. In most forms of congenital craniosynostosis, the coronal sutures are affected. However, in Carpenter syndrome, it is the midline sutures (particularly metopic and sagittal sutures) that are commonly fused. In severe cases, patients can present with cloverleaf skull (Jenkins et al. 2007). The calvaria may also be deformed, and unilateral involvement of the coronal or lambdoid sutures can produce asymmetry. Wormian bones have appeared in the anterior fontanel in a few cases. Mental retardation is a common characteristic of the syndrome, but patients with normal intelligence have been observed (Gorlin et al. 2001).

Hands and Feet

Syndactyly, polydactyly, and brachydactyly of the fingers and toes are typically present, and a characteristic feature of Carpenter syndrome is preaxial polydactyly of the toes (Robinson et al. 1985). Patients may also present with a single palmar crease, brachydactyly, and clinodactyly. Postaxial polydactyly and soft-tissue syndactyly between the third and fourth finger have been observed. Soft-tissue syndactyly may be present in the toes as well (Gorlin et al. 2001). Double toenails and whorls in the bones of the fingers and toes have also been noted (Robinson et al. 1985).

Craniofacial

Facial deformities including ocular, auricular, and mandibular deformities are common features. Ocular deformities include dystopia canthorum and mildly downslanting palpebral fissures, epicanthic folds, ▶ microcornea disease, corneal opacity, slight optic atrophy, and blurring of disk margins. Auricular deformities include preauricular fistula and low-set ears. Mandibular deformities include small mandible and arched or narrow palate, often leading to serious problems with dentition.

Cardiovascular

Congenital heart defects are common and include tetralogy of Fallot, ventral septal defect, atrial septal defect, and patent ductus arteriosus. Deformities of the great vessels and duplication of the superior vena cava have also been noted in a few cases.

Other Abnormalities

Other common features include obesity, hypogenitalism, and umbilical hernia. Common skeletal abnormalities include genua valga, patellar displacement, absent coccyx, spina bifida occulta, flaring of the ilia with poor development

of the acetabula, kyphosis, and scoliosis. Hydronephrosis, hydroureter, inguinal hernia, and accessory spleens have also been reported in a few cases. Patients usually have short necks, and many have short stature (below the 25th percentile), but may in certain cases be above the 60th percentile (Gorlin et al. 2001).

Diagnostics

Clinical observation and genetic testing can be used to confirm the diagnosis. CT scanning and MRI are performed prior to surgery. Fundoscopic examination is necessary to test for papilledema as a result of increased intracranial pressure (Davis et al. 2011).

Differential Diagnosis

Differential diagnoses include Apert syndrome, Bardet-Biedl syndrome, and Sanjad-Sakati syndrome (Gorlin et al. 2001). The critical period of development of Carpenter syndrome occurs between the 30th and 49th day of gestation, usually at a later stage than Apert syndrome but at an earlier stage than Bardet-Biedl syndrome, and therefore has overlap with characteristics of both disorders (Hidestrand et al. 2009). Examples of Carpenter syndrome include Summit syndrome and Goodman syndrome (acrocephalopolysyndactyly type IV) (Gorlin et al. 2001).

Prophylaxis

Unclear.

Therapy

Early surgical correction of craniosynostosis is performed before the 1st year of age to reduce intracranial pressure, enhance appearance, and prevent brain injury (though surgical intervention has not been shown to prevent mental retardation). Surgical intervention may also be necessary for syndactyly and polydactyly, umbilical hernia, and congenital heart defects among other abnormalities. Follow-up support by psychologists, genetic therapists, neurologists, ophthalmologists, otolaryngologists, cardiologists, and physical therapists may be necessary (Gorlin et al. 2001; Davis et al. 2011).

Prognosis

Prognosis of the disease is dependent on the management of associated symptoms. With proper surgical intervention and monitoring of other defects, children can live into adulthood. A single case of survival to adulthood with no surgical intervention has been reported. This case is a representation of the natural progression of Carpenter syndrome. A few of the problems that the patient suffered from included mental retardation, kyphosis, dental problems, congestive heart failure, chronic epiphora which lead to recurrent pneumonia, and optic nerve atrophy due to shallow orbits. The patient died at the age of 26 from complications related to Carpenter syndrome (Robinson et al. 1985; Hidestrand et al. 2009).

Epidemiology

Incidence of the syndrome is 1:1,000,000 of live births, and approximately 50 cases have been reported in the literature. Carpenter syndrome was first described in 1901 by Carpenter and characterized as a separate disorder by Tetamy in 1966 (Gorlin et al. 2001). Ten patients with the disease have been found to have Northern European descent. Both sporadic instances and cases of affected siblings have been reported (Jenkins et al. 2007).

Cross-References

▶ Microcornea

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Carpenter's Syndrome

▶ Carpenter Syndrome

Cat Scratch Disease

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Synonyms

Cat scratch fever; Inoculation lymphoreticulosis; Subacute regional lymphadenitis; Teeny's disease

Definition

Cat scratch disease (CSD) is an infectious disease commonly caused by *Bartonella henselae* (Ormerod and Dailey 1999). It is characterized by self-limited regional lymphadenopathy and can have visceral organ, neurologic, and ocular involvement.

Etiology

Cat scratch disease is primarily caused by *Bartonella henselae* (Cunningham and Koehler 2000). *B. henselae* is a gram-negative, nonmotile, aerobic pleomorphic bacillus (Florin et al. 2008). In the genus *Bartonella*, *B. bacilliformis*, *B. quintana*, *B. elizabethae*, *B. vinsonii*, and *B. koehlerae* may also cause CSD.

Cat exposure has been linked to CSD (Windsor 2001). Domestic cats are the natural reservoir and vectors of transmission of *B. henselae*. Transmission to humans occurs via a cat bite or scratch. Contact with kittens under 1 year of age has been documented in roughly 90–95% of CSD cases. Fleas have also been implicated in transmission of the bacteria and as the cause of CSD. Person-to-person transmission has not been documented.

Clinical Presentation

Individuals with cat scratch disease may present initially with a cutaneous lesion at the site of inoculation of the bacteria (Wear et al. 1983). The lesion usually develops after 3–10 days and generally evolves through vesicular, erythematous, and papular phases. Patients may present with regional, unilateral lymphadenopathy in the head, neck, or upper extremities about 1–7 weeks after animal contact (cat bite/scratch). Over 90% of cases include swollen lymph nodes. Additional symptoms include headache, fever, fatigue, abdominal pain, and possible rash. Very rarely is there extranodal dissemination of the disease.

Ocular involvement of CSD may take many forms, including Parinaud's oculoglandular syndrome, neuroretinitis, optic neuritis, and focal retinochoroiditis (Cunningham and Koehler 2000).

Parinaud's oculoglandular syndrome occurs in 2–8% of patients with CSD (Ormerod and Dailey 1999). Transmission may be directly from cat contact with the eye or hand-to-eye contact. The syndrome includes conjunctivitis, conjunctival granuloma, and adjacent preauricular lymphadenopathy (Lange and Gareis 2007). Eyelid swelling may be associated with severe reactions but

pain is uncommon. The primary granuloma disappears in several weeks, while regional lymphadenopathy resolves more slowly over months. It very rarely results in serious complications.

Neuroretinitis occurs in 1–2% of patients with CSD (Ormerod and Dailey 1999). It is an acute, unilateral visual loss from optic nerve edema associated with macular exudates. Visual acuity may vary from 20/20 to light perception and may worsen over the first several days. A relative afferent pupillary defect and a cecocentral, central, or arcuate visual field defect are typically present. CSD and *B. henselae* are the most common causes of neuroretinitis (Cunningham and Koehler 2000).

Many individuals with ocular manifestations of CSD may also develop retinal white dot syndrome (Ormerod and Dailey 1999). There are retinal infiltrates bilaterally that are round, white, and homogenous. They are a useful indicator of *B. henselae* infection and typically resolve without treatment in 2–3 weeks.

CSD can cause optic neuritis and must be considered on the differential when concerned for causes of optic neuritis.

Retinovascular syndromes are also associated with CSD. Cases of retinal vasculitis, peripapillary angiomatosis, and retinal arteriolar and venular occlusions have been reported in patients with CSD.

Diagnostics (Lab Diagnostics)

CSD is diagnosed typically from clinical findings and laboratory evaluation for confirmation. Exposure to cats is found in roughly 90% of patients with CSD (Cunningham and Koehler 2000).

The primary site of inoculation and regional lymphadenopathy must be determined for appropriate diagnosis (Ormerod and Dailey 1999). Lymph node biopsy and Warthin-Starry silver staining may be conducted if necessary. Further, blood culture samples may be taken to assess for *B. henselae. B. henselae* is a slow-growing, fastidious gram-negative bacterium that requires specific laboratory conditions for optimal growth. Blood culture samples should be collected in tubes containing EDTA to increase the probability of isolating *B. henselae*. Plating onto either chocolate agar or heart infusion agar enhances isolation of organisms.

Two serologic methods, the indirect fluorescence assay (IFA) and enzyme immunosorbent assay (EIA), may be used for diagnosis.

Additional lab tests – transient mild leukocytosis, with increased neutrophils and sometimes eosinophils, and elevated erythrocyte sedimentation rate – may occur.

Differential Diagnosis

Differential diagnosis include infectious and malignant causes of lymphadenopathy; malignant causes including lymphoma, Kaposi's sarcoma, and angiosarcoma; infectious including mycobacterial diseases, Lyme disease, coccidioidomycosis, *Nocardia*, *Bacillus anthracis*, syphilis, leishmaniasis, toxoplasmosis, and viral-associated lymphadenopathy; and noninfectious including cysts and sarcoidosis.

Prophylaxis

Unclear. Care with cats

Therapy

Most immunocompetent patients clear the disease on their own without medical intervention. Symptomatic treatment with analgesics or hot compresses may be recommended in patients with mild/moderate CSD (Windsor 2001).

If antibiotics are required, azithromycin, ciprofloxacin, rifampin, or doxycycline may be used (Ormerod and Dailey 1999). No optimal therapy is known for neuroretinitis.

Prognosis

Outpatient follow-up is recommended for assessing lymphadenopathy resolution. Overall,

there is a positive prognosis expected for patients (Ormerod and Dailey 1999). Depending upon severity of illness, immunocompromised patients may require hospitalization after CSD.

Epidemiology

Cat scratch disease appears to be transmitted primarily from a cat scratch/bite, but may be transmitted by fleabites (Windsor 2001). Cats are the main reservoir for *B. henselae*. Children and adolescents make up the majority of those infected by CSD. Immunosuppressed individuals are at higher risk of CSD and disseminated infection.

There are about 24,000 cases of CSD annually. CSD appears to have a broad international and North American distribution. The incidence is greater in regions with higher temperatures and humidity (e.g., Pacific Northwest, southeastern states). CSD tends to peak during the fall and early winter.

Cross-References

- ▶ Bartonella henselae, Cat Scratch
- ▶ *Bartonella henselae*, Cat Scratch
- ▶ Epidermoid Cysts
- ▶ Kaposi Sarcoma
- ▶ Lyme Disease
- ▶ Lymphoma: Definition
- ▶ Sarcoidosis
- ▶ Syphilis: Overview

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Cat Scratch Disease, Ocular Manifestations

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Synonyms

Cat scratch fever

Definition

Flulike illness associated with regional adenopathy and in some cases followed by neuroretinitis or Parinaud's oculoglandular syndrome (POGS). It is usually caused by *Bartonella henselae* which is transmitted by cats.

Background

Bartonella henselae, gram-negative rod, is the principal etiologic agent of cat scratch disease (CSD) and is associated with an expanding spectrum of ocular manifestations. *B. henselae* is 1 of 21 Bartonella species. Of these 21, 8 species have been found to cause human diseases, 4 of which (*B. henselae*, *B. quintana*, *B. grahamii*, and *B. elizabethae*) have been linked to ocular complications. CSD is a feline-associated zoonotic

disease, and cats are the primary mammalian reservoir of *B. henselae*.

Cat-to-cat transmission of *B. henselae* is mediated by the cat flea, but the role of fleas in transmission of infection to humans is unknown. CSD is transmitted to humans by the scratches, licks, and bites of domestic cats, particularly kittens. CSD follows a seasonal pattern, occurring predominantly in the fall and winter. Human-to-human transmission has not been reported.

Epidemiology

CSD is found worldwide and its prevalence has been estimated to be 9.3 per 100,000 persons.

Over 90% of patients report a history of having been scratched by a cat, often a kitten. Children younger than 10 years of age are particularly susceptible to CSD, constituting nearly 80% of cases.

Systemic Involvement

Systemic manifestations of CSD include a mild to moderate flulike illness associated with regional adenopathy that usually precedes the ocular manifestations of the disease. An erythematous papule, vesicle, or pustule usually forms at the primary site of cutaneous injury 3–10 days after primary inoculation and 1–2 weeks before the onset of lymphadenopathy and constitutional symptoms.

Ocular Involvement

Ocular involvement occurs in 5–10% of patients with CSD and occurring 1–4 weeks postinfection.

Anterior Segment

Approximately 4% of patients with symptomatic CSD suffered Parinaud's oculoglandular syndrome (POGS). The typical presentation of POGS includes conjunctival injection, serous discharge, and foreign body sensation. A granulomatous nodule, usually unilateral, develops in the palpebral conjunctiva, surrounded by follicles, intense chemosis, and injection. The nodule may be single, flat and large, or multiple and raised. The fornices and bulbar conjunctiva may also be involved. The granuloma disappears over the period of weeks and leaving no scar.

Corneal involvement usually consists of superficial punctate keratitis (SPK) but rarely causes significant keratitis.

Posterior Segment

Posterior segment involvement occurs in 1–2% of patients with CSD. The presentation is most often unilateral. Visual acuity loss varies between 6/6.5 and 6/60 or worse, 2–3 weeks after the onset of constitutional symptoms. Posterior segment includes neuroretinitis, retinitis, choroiditis, vasculitis, vascular occlusions, intermediate uveitis, panuveitis, and macular hole, and even serous retinal detachments have been reported.

Neuroretinitis

Neuroretinitis is a form of optic neuropathy characterized by optic disk swelling in the presence of a partial or complete macular star. Two to 4 weeks after the optic disk edema, there is an appearance of macular star. The development of the macular star is variable and may be partial or incomplete, usually resolving in approximately 8–12 weeks. When incomplete, a partial macular star is usually seen nasal to the fovea. Macular exudates remain stable for several weeks, after which a gradual regression begins, the most extensive macular exudates may take up to 12 months to resolve. Usually, patients regain most of their visual function; however, some patients suffer from decreased contrast sensitivity and dyschromatopsia.

Multifocal Retinitis and Choroiditis

Several forms of choroiditis and retinitis have been reported in CSD, some of which may mimic other retinochoroidal conditions. Diffuse choroiditis associated with CSD has been reported to cause multiple pinpoint leaks on fluorescein

angiography (FA). Multifocal retinitis in cat scratch disease may also present as bilateral, multiple, intraretinal white infiltrates, 100–300 μm in size, resembling one of the white dot syndromes. The white dots usually clear after 2–3 weeks without a trace. The presence of multifocal retinitis and/or choroiditis can be a clue to the diagnosis of *B. henselae* infection in cases of optic disk edema when associated with peripapillary serous retinal detachment, especially when subretinal or intraretinal exudates are absent.

Vasculitis and Vascular Occlusion

Ocular complications associated with retinochoroiditis in CSD may include vasculitis with arterial and/or venous occlusions causing severe visual loss.

Uveitis

Both intermediate uveitis and panuveitis have been reported in several cases with CSD. It has also been presumed that most patients with focal retinochoroiditis or neuroretinitis associated with CSD have a mild to moderate vitritis and sometimes significant non-granulomatous anterior uveitis.

Diagnosis

The diagnostic criteria for CSD include the following:

1. History of contact with a cat or kitten
2. Primary inoculation site either cutaneous or ocular
3. Positive serological tests – indirect immunofluorescence test (IFA) or enzyme-linked immunoassays (ELISA)

IFA is 88% sensitive and 94% specific for *B. henselae*, with titers of greater than 1:64 being considered positive. ELISA has a sensitivity for IgG of 86–95% and a specificity of 96%. Both IFA and ELISA tests depend on the robust immune response from the host. Because of that, the accuracy of both tests in immunocompromised patients is significantly lower.

Biopsy and Testing

The specimen can be obtained from the granulomatous conjunctival lesion or from infected lymph node. Testing includes:

1. Staining: Direct detection of bacteria by Warthin-Starry silver stain. This stain lacks species specificity.
2. Polymerase chain reaction (PCR): PCR testing for *B. henselae* was successfully used to identify B. henselae infection in specimens from conjunctiva and from lymph node biopsies and aspirates.
3. Cultures: Tissue or blood specimens can take up to 4 weeks before growth is detected on the culture media.

Treatment

In the majority of cases, CSD is a self-limiting illness that resolves completely within 2–4 months, with an overall excellent systemic and visual prognosis, even without treatment. The benign nature of CSD makes the necessity of antibiotic treatment doubtful. A variety of antibiotics, including doxycycline, erythromycin, rifampin, trimethoprim-sulfamethoxazole, ciprofloxacin, and gentamicin, have been used in the treatment of severe systemic or ocular manifestations, despite the fact that their efficacy has not been conclusively demonstrated. The duration of treatment is usually 2–4 weeks in immunocompetent patients and up to 4 months for immunocompromised patients.

Oral corticosteroids have been effective in reducing the inflammation and improving the visual function in cases with systemic and posterior ocular manifestations. However, the necessity of corticosteroids therapy in isolated POGS has not been established.

Differential Diagnosis

Syphilis, Lyme disease, tuberculosis, toxoplasmosis, toxocariasis, leptospirosis, salmonella, chicken pox (varicella), herpes simplex, Rocky

Mountain spotted fever, sarcoidosis, diabetic retinopathy, malignant hypertension, pseudotumor cerebri, and malignancies (especially lymphoma and tumor metastasis).

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Cat Scratch Fever

► Cat Scratch Disease, Ocular Manifestations
► Cat Scratch Disease

Cataract Eye Operation

► Cataract Surgery

Cataract Surgery

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Synonyms

Cataract eye operation

Definition

An operative treatment for removal of the eye's natural lens with cataract and implantation of an artificial intraocular lens implant (IOL).

Two techniques – phacoemulsification (incision 2–3 mm, foldable IOL) and conventional extracapsular cataract extraction (incision 10–12 mm, non-foldable IOL) – are currently the main types of cataract surgery extraction.

By reason of expense, the phacoemulsification technique is mostly practiced in industrial countries and the extracapsular cataract extraction (ECCE) in developing countries.

Epidemiology

Cataract surgery is the world's most frequently performed surgical treatment. The cataract surgery rate (CSR, the annual number of cataract operations performed per million population) varies in different countries.

The CSR of Europe countries and countries of the United States is 4000–5000 (source WHO). Although the CSR is often according to the economic and social development of countries, the WHO published a CSR about 3000 in India, for example, in the third-world countries up to 200.

Cataract surgery is commonly performed on an outpatient. Today the standard method is the extraction of cataract by phacoemulsification with implantation of a spherical intraocular lens.

History

The history of cataract disease goes back to ancient times. The beginning of surgical treatment was probably 800–600 BC in India: after scleral opening with an edged lancet, an inserted needle pushed the opacified crystalline lens into the vitreous body. This method is known as couching and was in basic principle practiced until the mid-nineteenth century.

The idea of a combined aspirating of cataract was firstly described 850 AC (Rhazes, Ammar).

After a better knowledge about the cataract's pathogenesis, Daviel created a surgical method similar to the established ECCE (extracapsular cataract extraction) in 1753.

Between 1753 and 1862, Pamard of Avignon (placing the surgical incision upper), Himly (introduction of pharmacological mydriasis), and Mooren (iridectomy to combat the complication of papillary block) affected the direction of cataract surgery.

The instrumental development was governed by De La Faye, Beer, and von Graefe.

Koller introduced cocaine as local anesthesia in 1884.

In 1949 Ridley began to implant artificial lenses. A further important step was managed by Barraquer in 1956 to describe the chemical zonulolysis using an enzyme (alpha-chymotrypsin).

Krawicz presented in 1961 a cryoextractor for intracapsular cataract extraction (ICCE). In the following year, Kelman introduced the Kelman phacoemulsification aspiration system in 1962–1967.

In 1980 Miller and Stegman use Healon to stabilize the anterior chamber.

The small incision surgery was developed in 1982 and the following years (Kraft, Sanders, Colvard, Fenzl, Girard).

Finally the last two milestones of the modern era were marked by Nagahara (1993, phaco-chop technique) and Agarwal (1998, bimanual microincisional phacoemulsification).

Clinical Features

It is referred to the articles specifically written that book.

Tests

The most important preoperative tests are listed below: investigation of anamnesis (general, drugs, ophthalmological); efficient examination of both eyes and refraction (including keratometry, uncorrected and best-corrected far and near visual acuity, if necessary retinometer visual acuity); quantification of contrast cognition and glaring, motility, and stereo tests and slit-lamp examination in mydriasis, tonometry, fundus examination (if necessary echography B-scan); and evaluation of the adequate intraocular lens implant (echography A-scan, biometry).

Differential Diagnosis

See "Treatment" section bottom.

Etiology

See "History" section above.

Treatment

The current preferred techniques in developed countries are phacoemulsification or extracapsular cataract extraction (ECCE) with inserting an intraocular lens implant (foldable or non-foldable lenses). In phacoemulsification technique, a small incision size is performed, whereas in ECCE the incision is larger and therefore usually depends on stitching.

The intracapsular cataract extraction (ICCE) is performed less today.

For the precise description of cataract surgery techniques, it is referred to the articles specifically written in that book.

Cross-References

- ▶ Biometry, Use and Principle of
- ▶ Continuous Curvilinear Capsulorhexis (CCC)
- ▶ IOL
- ▶ Phacoemulsification and Posterior Chamber Intraocular Lens (IOL) Implantation

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Cataract, Causes and Treatment

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Definition

Cataract is an opacification (clouding) of the crystalline human lens which can affect retinal image formation.

Etiology

Due to the multiplicity of possible causes and phenotypes the disease can be classified in several ways. A basic distinction can be made between congenital and acquired (e.g., senile, traumatic or uveitic, or glaucomatous) cataract.

Congenital cataract is an opacification of the lens which is already present at birth or manifests itself during the first year of life (Kuhli-Hattenbach et al. 2008). Possible causes are intrauterine infections, metabolic diseases, and a large variety of syndromes. The intrauterine infectious diseases most frequently responsible for a congenital cataract are rubella, measles, herpes simplex, varicella, Epstein-Barr virus, influenza, Syphilis, and Toxoplasmosis. Frequent genetic causes are familiar congenital cataract, galactosemia, Down's syndrome, trisomia 13, or Lowe's syndrome. The phenotype of the lenticular opacification is variable according to the part of the lens which is affected. As direct cause of the opacification are assumed oxidative stress and denaturation of lens proteins.

The most common form is, however, the senile cataract which occurs mainly in three manifestations: cortical, nuclear, or posterior subcapsular cataract. Not all types of cataract affect vision in the same way and to the same extent; central nuclear opacification, e.g., causes a reduction in visual acuity while early stages of posterior subcapsular cataract typically result in a strong sensation of glare (Sparrow et al. 1993; Sayegh et al. 2008).

Clinical Presentation

Main symptom of cataract is usually slow progressive loss of visual acuity. Effects of cataract are not limited to high-contrast visual acuity but can also compromise other visual qualities such as contrast sensitivity and glare.

Cataract of the lens nucleus can cause an increase in the optical power of the crystalline lens leading to a change in the overall refraction of the eye in the direction of myopia. Clinically, cataract is detected by slit-lamp examination of the anterior segment of the eye with dilated pupil. In that way, extent and localization of lens clouding and its relationship to the optical axis of the eye can be assessed.

Diagnostics

Cataract is most often diagnosed by slit-lamp examination of the anterior eye segment. For long-term evaluation and in cases of slight to moderate lenticular opacification, additional apparative diagnostics such as wavefront measurement and Scheimpflug photography can be helpful. However, a thorough examination of the anterior and posterior eye segment is mandatory to exclude coexisting other pathologies. In infantile and congenital cataract and those forms associated with extraocular diseases, additional examinations such as enzyme testing may be advisable.

Differential Diagnosis

The symptoms of cataract (loss of visual acuity and contrast sensitivity, glare) can be caused by many other ocular diseases such as corneal opacifications or retinal diseases. Characteristic for cataract are the usually slow onset of the symptoms and the typical findings in slit-lamp microscopy.

Prophylaxis

Among the identified etiological factors of cataract are prominent old age, oxidative stress, and exposure to radiation. Protection from excessive UV radiation and a generally healthy lifestyle (e.g., avoidance of smoking) seem to be beneficial. So far, no drugs have been proven effective for the prevention of cataract.

Therapy

An effective conservative therapy with drugs does not exist. Therefore, standard treatment consists of removal of the lens material from the lens capsule and implantation of an artificial intraocular lens (IOL) (Sayegh et al. 2008). The current state-of-the-art method for removal of the lens is ultrasound phacoemulsification. Special attention is paid to minimally invasive surgical techniques in order to prevent unwanted effects and complications such as surgically induced astigmatism or intraocular microbial (usually bacterial) infections (endophthalmitis). Modern IOL optics can achieve high postoperative optical quality and high patient satisfaction.

Prognosis

If not treated adequately (i.e., surgically), the lenticular opacification will progress with consecutive further deterioration of vision. In cases without additional ocular pathologies, cataract surgery with implantation of an intraocular lens gives excellent results and can fully restore vision.

Epidemiology

Cataract is the most frequent cause of blindness worldwide. In the USA, in 42% of persons between the ages of 52 and 64, 60% of those between the ages 65 and 74, and 91% of those between the ages of 75 and 85 age-related opacifications of the crystalline lens could be detected. The estimated worldwide number of cataract operations per year is six to ten millions. The cataract surgical rate (CSR, the number of cataract surgeries per one million inhabitants) is variable from one country to another. According to the WHO, it is at a very high level of 4000–5000 in the USA and Europe while it is about 3000 in threshold states like India and only 200 in third world countries due to differences in the quality of medical care. The most frequent variant is the age-related cataract which occurs from the sixth decade of life onwards.

Cross-References

- ▶ Cataract Surgery
- ▶ Lens Capsule
- ▶ Phacoemulsification and Posterior Chamber Intraocular Lens (IOL) Implantation
- ▶ Scheimpflug Imaging
- ▶ Wavefront Measurement

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Catarrhal (Marginal Corneal) Infiltrates

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Synonyms

Marginal keratitis; Microulcerative peripheral keratitis; Staphylococcal hypersensitivity keratitis; Staphylococcal marginal disease

Definition

Catarrhal infiltrates are a subtype of peripheral keratitis believed to be secondary to hypersensitivity to staphylococcal antigens.

Etiology

Catarrhal ulceration is thought to be a sterile, type III immune response in which staphylococcal antigens react with antibodies along the limbus, resulting in immune complexes. The limbus is especially prone to such inflammation because of its proximity to vascular arcades that provide the area with additional inflammatory mediators (Stern 2005).

Clinical Presentation

Symptoms of catarrhal ulceration often include pain, photophobia, and history of ocular redness. Because blepharitis often occurs simultaneously, patients may also notice a more chronic history of irritation and crusting. Examination findings are most prominent on the lids, conjunctiva, and cornea. Lids will often show signs of staphylococcal blepharitis which include collarettes surrounding lashes, redness along lid margins, and occasionally microulcerations near lash bases. In marginal keratitis, the conjunctiva is mildly injected. Classic corneal findings in catarrhal ulceration include small white infiltrates adjacent to the limbus with an intervening clear zone. These opacities most commonly occur in clock hours of the cornea with frequent exposure to antigen-rich eyelid margins (2, 4, 8, and 10 o'clock). Corneal epithelium is largely intact over these lesions although variable degrees of staining may be present. Oftentimes, there will be evidence of prior catarrhal ulceration in the fellow eye (Stern 2005; 2013–2014 Basic and clinical science course).

Diagnostics (Lab Diagnostics)

Catarrhal ulceration is usually a clinical diagnosis made by the presence of typical findings. In cases where there is concern for infectious keratitis (cases with more prominent epithelial defect, suppurative inflammation, or other risk factors), one should consider performing corneal cultures to rule out infectious keratitis.

Differential Diagnosis

There are numerous potential causes of microulcerative peripheral keratitis. Certain topical medications may induce a hypersensitivity reaction that may have a similar appearance. Common culprits include topical anesthetics, aminoglycosides, epinephrine, and phenylephrine. Typically hypersensitivity to topical medication will occur in close time proximity to instillation of the offending agent (Stern 2005). Contact lens wear can also initiate small, circumscribed infiltrates adjacent to the limbus in some patients. These lesions are often associated with extended wear soft contact lens usage. Phlyctenulosis is a disorder of the peripheral cornea also thought to be secondary to an exaggerated immune response to staphylococcal antigens along the corneal limbus. Patients with phlyctenule often present with findings of staphylococcal blepharitis and inflamed conjunctiva. Instead of circumscribed infiltrates, these patients possess an elevated white lesion comprised of a mixture of various inflammatory cells. Rosacea blepharitis can induce a peripheral keratitis marked by corneal neovascularization, corneal infiltration along the edges of offending blood vessels, and punctate epitheliopathy.

Eyelids in these patients will often show evidence of posterior blepharitis and meibomian gland dysfunction. Skin changes in rosacea can be helpful in differentiating rosacea keratitis from catarrhal ulceration and often include malar erythema, facial telangiectasias, and corresponding dermatologic lesions. Finally, any area of significant ulceration associated with significant inflammation, purulence, and pain should be evaluated for infectious or peripheral ulcerative keratitis (Stern 2005).

Prophylaxis/Therapy

The mainstay of treatment for catarrhal ulceration is topical steroid. A common regimen includes a low-dose steroid such as loteprednol 0.2% four times daily until disease resolution. A topical antibiotic such as Polytrim is also commonly employed to prevent infection. Treatment for concomitant staphylococcal blepharitis is also important for long-term prophylaxis and may include lid hygiene measures and a topical antibiotic ointment such as bacitracin (Stern 2005; 2013–2014 Basic and clinical science course).

Prognosis

Catarrhal infiltrates often respond quickly to the above treatment regimen. Moreover, if left untreated catarrhal infiltrates will resolve over the course of several weeks. Flares can be recurrent and can involve the fellow eye in patients prone to staphylococcal blepharitis (Stern 2005; 2013–2014 Basic and clinical science course).

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Cavernous Hemangioma

▶ Vascular Tumors Disease of the Conjunctiva

Cavernous Sinus Anatomical Boundaries and Contents

▶ Cavernous Sinus Anatomy

Cavernous Sinus Anatomy

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Synonyms

Cavernous sinus anatomical boundaries and contents

Definition

The cavernous sinus is a dural venous sinus located lateral to the sella turcica. Venous drainage from the superior and inferior ophthalmic veins empties into the cavernous sinus, and the cavernous sinus itself drains into the superior and inferior petrosal sinuses, as well as the pterygoid plexus. Structures contained within the cavernous sinuses include CN III (and associated parasympathetic fibers), IV, V1, V2, VI, the internal carotid artery (ICA), and associated ocular sympathetic fibers.

One potential danger zone for bacterial spread is formed between the tip of the nose and the two labial angles. Venous drainage from this danger zone leads to the pterygoid plexus through the deep facial veins. Due to the valveless connection between the cavernous sinus and pterygoid plexus, bacterial infection and septic thrombosis of the cavernous sinus may result from a cutaneous infection in this danger zone.

A cavernous sinus syndrome can be due to any lesion in the cavernous sinus (e.g., infectious inflammatory, neoplastic, fistula, aneurysm) producing a multitude of clinical symptoms including ptosis, anisocoria, or diplopia from ocular motor cranial nerve (CN III, IV, VI) involvement, trigeminal pain or numbness (V1, V2), or headache from the resultant inflammation caused by the infection and septic thrombosis.

Cross-References

- ▶ Carotid Cavernous Fistula
- ▶ Dural Sinus Thrombosis

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Cavernous Sinus Syndrome

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Synonyms

Jefferson syndrome

Definition

Cavernous sinus syndrome (CSS) is defined by signs and symptoms (see cavernous sinus anatomy) related to cavernous sinus pathology and include cranial neuropathies, ophthalmoplegia, proptosis and orbital congestion, orbital or facial pain, trigeminal sensory loss, and ocular sympathetic disturbance such as Horner syndrome. CSS can be caused by multiple conditions resulting in pathology of the cavernous sinus or the structures within. CSS can be divided into four types based on etiology: infection, noninfectious inflammation,

vascular lesion, and neoplasm. Infectious diseases include cavernous sinus thrombophlebitis, actinomycosis, rhinocerebral mucormycosis, and aspergillosis. Noninfectious inflammatory conditions include Tolosa-Hunt syndrome and idiopathic or secondary inflammatory syndromes. Different types of CSS vascular lesions include aneurysm of the internal carotid artery (ICA), carotid-cavernous fistula, and dural arteriovenous fistula. Finally, neoplastic lesions in the cavernous sinus include primary tumors, intracranial tumors directly invading the cavernous sinus, perineural spread of the head and neck tumors, or hematogenous spread of distal tumors.

Etiology

There are several etiologies of CSS and an understanding of the anatomy is critical. Located lateral to the sella turcica, the cavernous sinus is a trabeculated venous cavity invested by the dura mater. It contains several vascular and neural structures, including the ICA and sympathetic fibers that traverse it. The cavernous sinus also contains cranial nerves (CN) III, IV, V1, V2, and VI. CN VI (i.e., abducens nerve) runs lateral to the ICA within the cavernous sinus, while CN III, IV, V1, and V2 course in the lateral wall of the cavernous sinus between the two dural layers.

The cavernous sinus normally receives drainage from the superficial Sylvian vein, the superior and inferior ophthalmic veins, and the sphenoparietal sinus. Laterally, the middle meningeal vein drains into the cavernous sinus. The cavernous sinus then posteriorly drains into the superior and inferior petrosal sinuses. Anastomoses connecting the two cavernous sinuses include a basilar plexus of the veins and an intercavernous sinus and allow the progression of unilateral lesions into a bilateral lesion.

Etiologically cavernous sinus syndrome can be divided into infectious, noninfectious inflammatory, vascular, and neoplastic categories as described previously and are discussed more in depth below:

I. CSS Infectious Diseases
   1. Cavernous sinus thrombophlebitis is caused by bacterial or fungal invasion secondary to paranasal sinus infection, orbital cellulitis, or midface infection. The most common causative organism is *Staphylococcus aureus*, although other organisms including *Pneumococci* and fungi can also be seen. Cavernous sinus thrombophlebitis most frequently occurs in patients with immunosuppression or poorly controlled diabetes.
   2. *Actinomyces* accesses the central nervous system via direct extension from the ear or sinuses, or it may reach the central nervous system via hematogenous spread. Actinomycosis is rare and usually seen in immunocompetent men.
   3. Rhinocerebral mucormycosis fungi usually gains access to the nasal cavity and paranasal sinuses through inhalation and cause necrotizing vasculitis and thrombosis in the nose and sinuses. Infection may then directly extend through the skull base or indirectly access the central nervous system via the ICA and cavernous sinus. Rhinocerebral mucormycosis is seen in immunocompromised and diabetic patients.
   4. Aspergillosis infection usually occurs through hematogenous spread or direct extension of paranasal sinuses, middle ear, or orbital infection. It invades blood vessels and is most commonly seen in immunocompromised patients.

II. CSS Noninfectious Inflammation
   1. Tolosa-Hunt syndrome is characterized by nonspecific granulomatous inflammation in the anterior cavernous sinus, superior orbital fissure region, or orbital apex. However, the exact etiology is unknown.
   2. Inflammatory pseudotumor is characterized by idiopathic inflammatory lesions of the skull base and is characterized by inflammatory cell infiltration and a variety of fibrotic responses.

III. Vascular
    1. Aneurysm of the cavernous segment of the ICA could compress adjacent structures leading to specific symptoms. In adults, they are the most common cause of non-neoplastic parasellar masses.
    2. Carotid cavernous fistula and dural arteriovenous fistula are pathological shunts where the arterial blood flows from the carotid artery into the cavernous sinus, creating a direct communication between arterial and venous blood flow. They are divided into direct and indirect shunts. Direct shunts are most commonly caused by trauma leading to a tear in the ICA, whereas indirect shunts result from tears in the meningeal branches of the carotid artery.
IV. Neoplasm
    1. Intracranial tumor such as pituitary adenoma can directly invade into the cavernous sinus.
    2. Primary tumors can directly arise from the cavernous sinus, such as meningiomas and neurogenic tumors.
    3. Head and neck malignancy can spread to the cavernous sinus via perineural invasion.
    4. Metastatic tumors could originate from distant sites, including the lungs, breasts, and prostate gland.

Clinical Presentation

Clinical presentations of CSS include cranial neuropathies, ophthalmoplegia, proptosis and orbital congestion, orbital or facial pain, trigeminal sensory loss, and sympathetic disturbance such as Horner's syndrome. However, the exact clinical presentation depends on the underlying pathology. For example, cavernous sinus thrombosis may have initial localizing features of unilateral chemosis, periorbital edema, and eyelid swelling. Ophthalmoplegia and exophthalmos may follow as retrobulbar pressure increases, and symptoms may progress to sluggish pupillary reaction, development of extraocular muscle palsies, and diminished acuity.

On the other hand, noninfectious inflammatory causes such as Tolosa-Hunt syndrome (idiopathic granulomatous painful, steroid-responsive CSS) result in painful ophthalmoplegia that is peri- or retro-orbital, severe, and typically lancinating in quality. Meanwhile, vascular causes such as direct carotid-cavernous fistula can present with the classic symptom triad of chemosis, pulsatile exophthalmos, and bruit. But if the underlying vascular defect is an indirect carotid-cavernous fistula, symptoms are insidious in onset and may be variable.

The clinical presentation of neoplastic cavernous sinus syndrome is also variable depending on the type of tumor, location of the tumor, rate of tumor growth, and structures affected by the tumor. Ocular motor cranial neuropathy will be present if the underlying pathology affects CN III, IV, or VI. Trigeminal neuropathy would be present if the ophthalmic (V1) or maxillary (V2) divisions of the trigeminal nerve are affected.

Diagnosis

The diagnosis of CSS is dependent on the underlying etiology, but magnetic resonance (MR) imaging, computed tomography (CT), and cerebral angiography each play a role. The diagnosis of infectious CSS is primarily based on clinical information, although CT and MR imaging can provide direct signs such as changes in signal intensity and size of the cavernous sinus. Imaging could also provide indirect signs including dilation of tributary veins and exophthalmos that clue one to an infectious CSS. Specific bacterial and fungal causes may have different characteristics on imaging.

As another example, the diagnosis of Tolosa-Hunt syndrome is based on exclusion of other traumatic, infective, vascular, neoplastic, metabolic, and inflammatory causes. Further diagnostic criteria include retro-orbital pain that may proceed to ophthalmoplegia and ophthalmoplegia

with or without periarterial sympathetic fiber and optic nerve involvement. Nonspecific inflammatory lesions in the anterior cavernous sinus, the superior orbital fissure, or the orbital apex may also be visualized on MR imaging in Tolosa-Hunt syndrome.

Vascular lesions including thrombosis, aneurysm, and fistula may be well demonstrated using CT angiography initially, but cerebral angiography is the gold standard diagnostic tool for detailed morphology and flow patterns. In addition, endovascular therapy may be directed at the time of cerebral angiography. If mass is suspected, MR imaging is usually the preferred diagnostic method.

Therapy

Treatment must be targeted at the particular underlying cause of CSS. In general, infectious causes require prompt administration of broad-spectrum antibiotics and may require draining of any abscess cavities. Identifying the causative organism is also essential in administering the correct treatment. As for primary cavernous sinus thrombosis, anticoagulant therapy may be beneficial. In Tolosa-Hunt syndrome, patients are universally responsive to corticosteroid treatment. If the underlying cause is vascular as in the cases of fistulas or aneurysms, endovascular therapy may be required. Finally, the management of neoplastic CSS is difficult due to the significant cranial nerve morbidity in surgeries, and exact treatment will be case specific.

Prognosis

Given the broad range of etiologies, the prognosis of CSS is also dependent on the underlying pathology. For example, treatment of septic cavernous sinus thrombophlebitis usually leads to cranial nerve palsy's resolution. However, if visual loss is present, it will likely remain, as it suggests infarction of the retro-orbital portion of the optic nerve. On the other hand, following successful endovascular treatments, patients with carotid-cavernous fistula usually experience a resolution of symptoms. The prognosis of visual loss due to the carotid-cavernous fistula will depend on the underlying pathology of the visual loss. Finally, after corticosteroid treatment, most patients with Tolosa-Hunt syndrome experience a resolution of symptoms, though spontaneous remissions may also occur.

Differential Diagnosis

1. Diabetic ophthalmoplegia
2. Giant cell arteritis
3. Ophthalmoplegic migraine
4. Posterior fossa aneurysm

Cross-References

- ▶ Aneurysms
- ▶ Arteriovenous Malformations (AVMs)
- ▶ Carotid Cavernous Fistula
- ▶ Cavernous Sinus Anatomy
- ▶ Cerebral Venous Sinus Thrombosis (CVST)
- ▶ Ring Sign, in Idiopathic Orbital Inflammation

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Cavernous-Carotid Fistula

▶ Carotid Cavernous Fistula

CC Fistula

▶ Carotid Cavernous Fistula

CCF

▶ Carotid Cavernous Fistula

CCT

▶ Central Corneal Thickness

Cefuroxime

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Definition

Second-generation cephalosporin antibiotic.

Indication

Prophylaxis of postoperative endophthalmitis after cataract surgery, therapy of bacterial keratitis.

Contraindication

Allergy against second-generation cephalosporin antibiotics.

Use and Dosage

Cefuroxime disrupts the synthesis of the peptidoglycan layer of bacterial cell walls. Intracameral administration of cefuroxime (1 mg in 0.1 mL normal saline) at the end of cataract surgery was found to be effective in reducing the risk for endophthalmitis after cataract surgery by phacoemulsification. Use of cefuroxime eyedrops (1–5%) has been described in the therapy of bacterial keratitis. However, the formulation is not commercially available.

Adverse Reactions

In systemic use, diarrhea, nausea, vomiting, headaches/migraines, dizziness electrolyte disturbances, and abdominal pain have been described. Excessive doses of intracameral antibiotic agents or inadequate preparation may cause toxic anterior segment syndrome.

Cross-References

▶ Antibiotics for Eye Infections
▶ Cataract Surgery
▶ Intracameral Antibiotics
▶ Toxic Anterior Segment Syndrome

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Cellophane Maculopathy

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Synonyms

Epiretinal membrane; Macular pucker; Pseudo macular hole; Preretinal macular fibrosis; Preretinal macular gliosis; Preretinal vitreous membranes; Silk-screen retinopathy; Surface-wrinkling maculopathy

Etiology

Cellophane maculopathy refers to a membrane present at the surface of the retina overlying or surrounding the foveal pit. It is composed of newly formed collagen (mainly types II and IV) and basement membranes, as well as a population of spindle-shaped cells that are GFAP and AE1/AE3 positive, suggesting a glial origin (Fig. 1). The cells have been referred to in the literature as laminocytes, myofibroblasts, or histiocytes. The above description refers to idiopathic membranes with no associated underlying ocular pathology. In cases associated with retinal tears or detachment, retinal pigment cells are invariably present. In membranes associated with diabetes, neovascular stromal tissue is observed. Following trauma, or ocular inflammation, macrophages and inflammatory cells are seen alongside the laminocytes.

Laminocytes are thought to populate the retinal surface prior to a separation of the posterior vitreous, at a time when vitreoretinal traction is causing some mechanical stress to the foveal area. Collagen deposition likely begins at this time. However, when most idiopathic membranes are diagnosed or when therapy is instituted, a posterior vitreous detachment has already occurred. As collagen and extracellular matrix is deposited, the cells cause a contraction of the retinal surface. This in turn causes distortion of the surface vessels that are pulled centripetally toward the center of one or more traction points. With more intense traction, deeper retinal structures are affected leading to loss of retinal integrity and the appearance of cystic structures or edema. Involvement of outer retinal structures, in particular the photoreceptors, will lead to alteration in visual perception.

Clinical Presentation

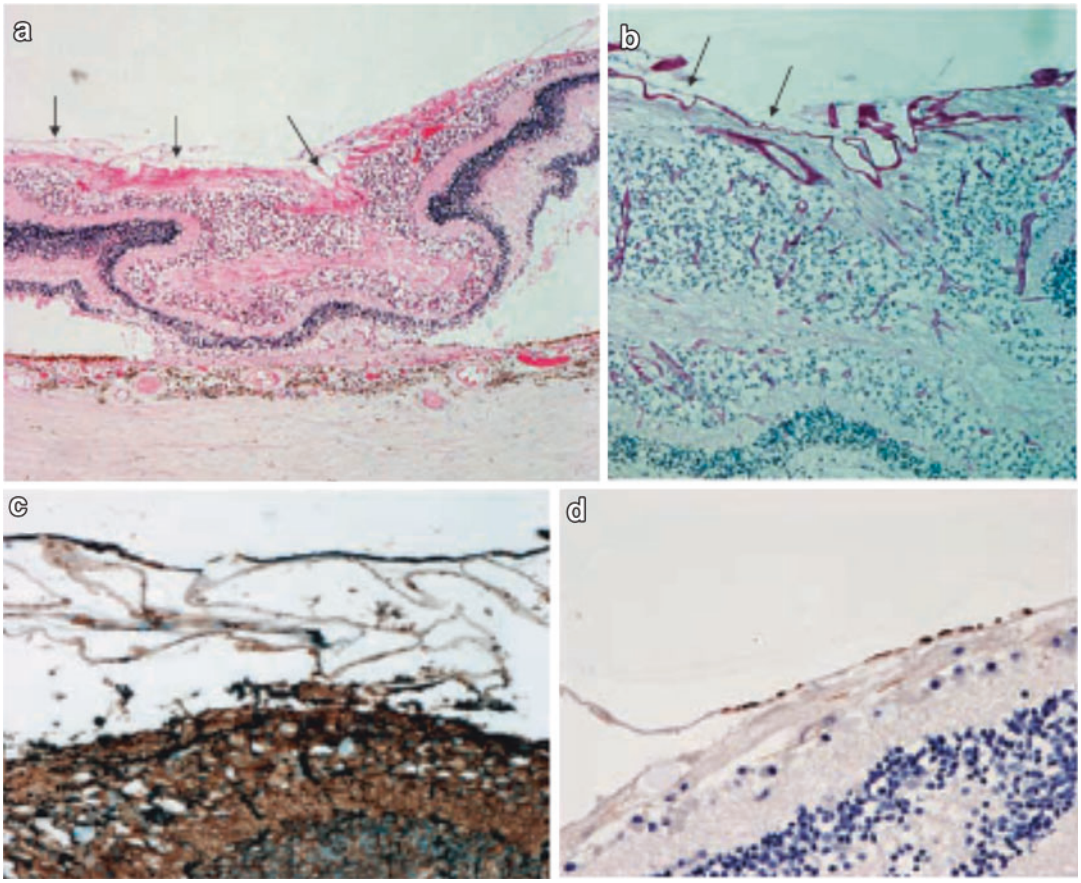
Patients usually complain of distorted lines or images. Straight lines or objects are wavy, while letters have abnormal shapes. Initially, visual acuity remains excellent, but as the distortion worsens, vision begins to decrease. This stage is often associated with the appearance of macular edema as the traction on the retina causes structural retinal changes. These can be seen by biomicroscopy, fluorescein angiography, or optical coherence tomography (OCT).

Diagnostics

The patient can indicate the location of his distortions on an Amsler grid, while an M-chart can help define the severity of the distortion and follow its evolution. On biomicroscopy, a glistening structure is seen at the surface of the macula, while it is absent in the surrounding retina. This glistening caused by the membrane leads to the name cellophane maculopathy. It is often associated with vascular distortion and wrinkling, as vessels in and surrounding the membrane are drawn to traction points within. The membranes can be documented by fundus photography and multispectral scanning laser ophthalmoscopy (Fig. 2). The latter may be particularly useful in identifying subtle membranes.

Fluorescein angiography allows one to document the degree of vascular compromise as affected vessels become permeable leading to the appearance of macular edema.

On longitudinal OCT, above the plane of the retina, a reflective layer of variable thickness and density is observed. It is associated with undulations of the retina, more prominent in superficial layers, involving deeper layers as the membrane causes more centripetal traction (Fig. 3). On



Cellophane Maculopathy, Fig. 1 Sections from post-mortem globes. (**a**–**c**) A case of mascular pucker. The retinal surface can clearly be seen in (**a**) with a typical CM type ERM, including hyperconvoluted ILM present on the retinal surface (arrows) (H&E). The ILM is more clearly demonstrated with the DPAS stain in (**b**), and the GFAP immunocytochemistry stain shows strong positivity in the laminocytes (**c**). (**d**) Another case with a PVD, in which laminocytes are clearly visible on the retinal surface, and staining positively for cytokeratin AE1/AE3. Original magnifications (**a**) ×100; (**b**) ×200; and (**c**, **d**) ×400. (Taken from Eye (2008) 22:1310–1317 Snead DRJ et al.)

transversal OCT scans, the membrane can be seen as a highly reflective surface above the plane of the retina. When looking at the retinal surface, folds are visible radiating out of individual traction points (Fig. 4).

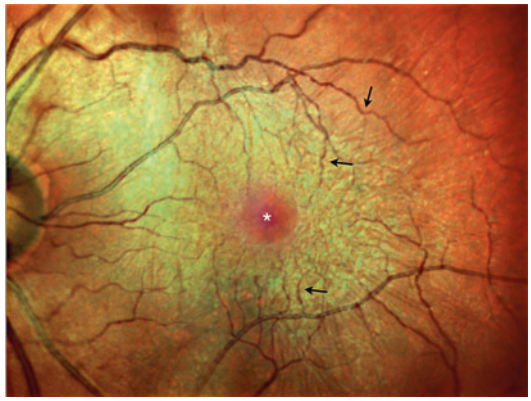
Differential Diagnosis

Cellophane maculopathy is idiopathic. Other etiologies or associations include:

- Retinal detachment or tear
- Proliferative vitreoretinopathy (PVR)
- Proliferative diabetic retinopathy (PDR)
- Retinal vein occlusion
- Diabetic macular edema
- Uveitis
- Ocular trauma

Prophylaxis

There is no proven prophylaxis. However, the presence of vitreomacular traction is felt to be a major contributor to the formation of preretinal membranes, particularly in pseudophakic patients. A significant increase in the incidence of membranes following cataract surgery has been observed in the 6 months following surgery.

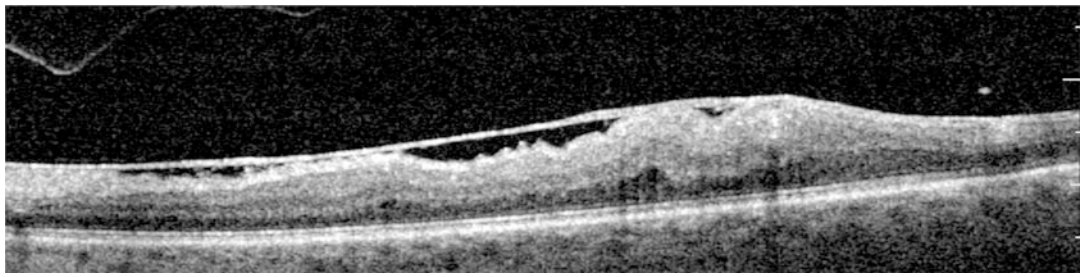


Cellophane Maculopathy, Fig. 2 Multispectral image of an epiretinal membrane. Vessels are tortuous (*arrow*) or drawn toward one another arrowhead. This particular membrane skirts around the fovea forming what is referred to as a pseudohole (*asterik*)

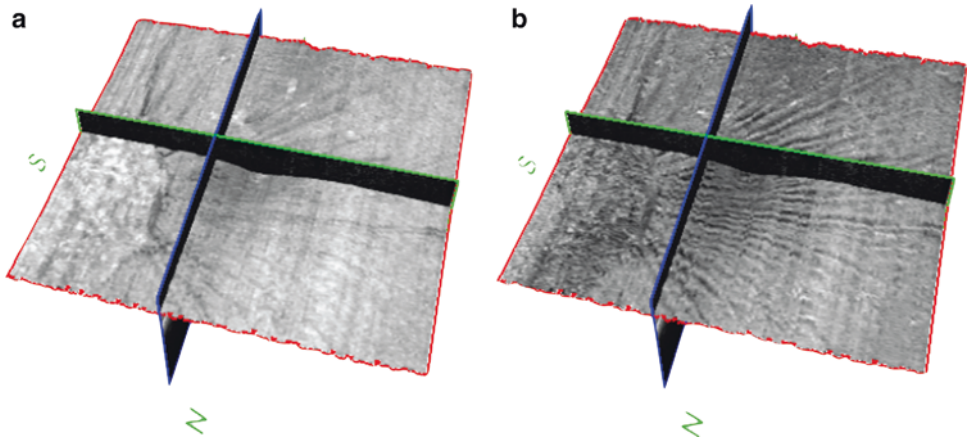
Inducing a medical or surgical release of vitreoretinal traction may limit the appearance of these membranes, but this approach has not so far been proven effective. The growth of membranes can be minimized by limiting or treating any concurrent inflammatory response present in the eye.

Therapy

Not all membranes require therapy. If they do not cause visual loss or distortion, treatment is usually not required. Surgical removal is the only effective therapy. Following removal of the pre-macular vitreous by means of a pars plana vitrectomy, the membrane is peeled from the retinal surface with or without the use of a staining agent (chromovitrectomy).



Cellophane Maculopathy, Fig. 3 Longitudinal OCT scan through the macula showing a thick membrane on the surface of the retina with wrinking of several underlying layers. The posterior surface of a detached vitreous is visible in the upper left corner of the image



Cellophane Maculopathy, Fig. 4 Transversal OCT scan showing in **a** the surface of the membrane above the retinal plan as a highly reflective layer. In **b**, with the scan set at the level of the retina, the radiating folds in the retina are clearly visible, extending a considerable distance from the site of the membrane

Prognosis

Most epiretinal membranes are found incidentally during an ocular exam, as is frequently seen with peri-macular membranes. Only a minority of membranes progress causing more traction on the retinal surface, usually under the influence of an external stimulus as indicated above.

Epidemiology

The prevalence varies with age and is considered to be between 7% and 12% overall. Rarely observed below the age of 40, it is reported to be present in 15% of patients above 70 years of age. Over age 50, in a healthy population, the 5-year incidence is reported to be as high as 5%. Following cataract surgery, the prevalence is said to double over a 6–12-month period.

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Cellulitis, Preseptal, *Haemophilus* Causing

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Synonyms

Periorbital cellulitis

Definition

A soft tissue infection of the eyelids that has not extended beyond the septum and into the orbit. Prior to the advent of the *Haemophilus influenzae* type B (HiB) vaccine, this organism caused many pediatric cases of preseptal and orbital cellulitis.

Etiology

A broad variety of insults can lead to the development of preseptal cellulitis. The most common among these in the pediatric population is ethmoid sinusitis. Other causes include hordeola, infectious dacryoadenitis, dacryocystitis, trauma, insect bites, and periocular surgery.

Clinical Presentation

Patients with preseptal cellulitis present with swollen, erythematous eyelids. Depending on the cause of the infection, other classical stigmata may also be seen (e.g., the "S-shaped" upper eyelid deformity of dacryoadenitis). While it may be difficult to examine the eye due to swelling – particularly in uncooperative children – there should be no significant changes in visual acuity, motility deficits, pain with eye movement, proptosis, injection, or chemosis. These signs should prompt the clinician to suspect a true orbital cellulitis.

Diagnosis

Preseptal cellulitis is a clinical diagnosis. Nevertheless, it is often prudent to obtain dedicated orbital imaging in order to assess the condition of the sinuses if the cause of infection is not immediately apparent. In borderline cases or those in which the eye cannot be assessed adequately due to lack of cooperation, imaging is imperative to exclude orbital cellulitis.

If present, secretions or discharge should be cultured. Inpatient treatment with intravenous antibiotics is rarely necessary, but blood cultures are often obtained in this setting. *Haemophilus* bacteremia was often associated with preseptal

and orbital cellulitis prior to introduction of the HiB vaccine, and a high index of suspicion should be maintained in individuals with an uncertain vaccination history.

Differential Diagnosis

Orbital cellulitis
Irritant or allergic contact dermatitis
Herpes simplex or zoster
Blepharochalasis
Secondary inflammation due to ocular pathology
Rhabdomyosarcoma
Metastatic neuroblastoma
Ruptured dermoid

Prophylaxis

No generalized prophylaxis. Patients with chronic sinusitis may benefit from medical or surgical therapy.

Therapy

Preseptal cellulitis is typically treated with oral antibiotics that cover the spectrum of commonly associated microbes (e.g., amoxicillin/clavulanic acid). A lid abscess increases the pretest probability of infection with community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA), and coverage should be adjusted accordingly. Symptomatic relief may be obtained with cold compresses and Tylenol. In borderline cases, or when *Haemophilus influenzae* type B is suspected based on vaccination history, admission for imaging, blood cultures, and intravenous antibiotics may be prudent. Nasal decongestants and saline rinses are often added when sinusitis is the underlying cause. Close follow-up is required to exclude progression to orbital cellulitis.

Prognosis

In general, the prognosis for preseptal cellulitis is excellent with timely and appropriate therapy. *Haemophilus influenzae* type B was frequently associated with childhood bacteremia, epiglottitis, otitis, and meningitis; prognosis is more guarded in such cases and careful management is required.

Epidemiology

Preseptal cellulitis may affect any age group, but is particularly common in younger children. Prior to the advent of the HiB vaccine, *Haemophilus*-related infections were commonly seen in those aged 5 and younger.

Cross-References

- ▶ Dacryoadenitis
- ▶ Dacryocystitis
- ▶ External Hordeolum (Stye)
- ▶ Gram-Negative Bacteria
- ▶ Gram-Positive Bacteria
- ▶ Haemophilus influenzae, Conjunctivitis

Further Reading

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Donahue SP, Schwartz G (1998) Preseptal and orbital cellulitis in childhood. A changing microbiologic spectrum. Ophthalmology 105(10):1902–1905, discussion 1905-6

Center-Involved Diabetic Macular Edema

▶ Diabetic Macular Edema

Central Angiospastic Retinopathy

▶ Central Serous Chorioretinopathy/Choroidopathy

Central Anisocoria

▶ Physiologic Anisocoria

Central Cloudy Dystrophy of François

▶ Corneal Dystrophies
▶ François, Central Cloudy Dystrophy

Central Corneal Clouding

▶ Sattler's Veil (Central Epithelial Edema)

Central Corneal Thickness

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Synonyms

CCT; Central pachymetry; Corneal thickness

Definition

The thickness of the cornea at its center.

Basic Characteristics

The central corneal thickness (CCT) of a normal and healthy cornea ranges from 450 to 650 µm (Doughty and Zaman 2000). It can be thinner in ectatic corneal diseases such as keratoconus, pellucid marginal degeneration, and iatrogenic keratectasia and after surgical tissue ablation. CCT is increased in case of corneal edema (e.g., endothelial dystrophy), in cases of cornea plana, and other corneal dystrophies. Also after lamellar and penetrating keratoplasty, CCT can be increased.

Measurement of the corneal thickness is called pachymetry (*gr.* παχύς: thick). There are different techniques for measuring CCT. The oldest technique uses an optical device of planparallel plates for the slit lamp microscope. CCT could be read indirectly by correctly positioning the two plates relatively to each other. The most widespread used technique and still the gold standard for measuring CCT is ultrasound pachymetry. Optical sections of the cornea could also be done with Scheimpflug photography and optical coherence tomography. Thus, pachymeters based on these principles are available both as standalone unit and integrated in multifunction devices. Advantages of optical pachymeters are their non-invasiveness and the possibility of mapping thickness over the entire cornea.

CCT measurements have clinical relevance in glaucoma detection and refractive surgery. Eyes with thin corneas are more prone to develop glaucoma (Gordon et al. 2002). Moreover, Goldmann applanation tonometry readings are lower than the nominal value if the cornea is thin (Ehlers et al. 1975). In corneal refractive surgery, knowing corneal thickness is essential for treatment planning. In most cases, the CCT is sufficient. Recent studies revealed not only a thinner absolute CCT in keratoconus eyes but also a different ratio between central and peripheral corneal thickness (Ambrósio et al. 2006; Bühren et al. 2010). CCT is not only a limiting parameter for treatments (the residual stromal bed thickness should not be below 250 µm) but also a useful metric for the detection of early keratoconus. However, for keratoconus detection, CCT needs to be always interpreted in conjunction with other data since there is no threshold value below which a cornea is considered a keratoconus cornea.

Cross-References

▶ Corneal Ectasia
▶ Developmental Glaucoma
▶ Keratoconus
▶ Pellucid Marginal Degeneration
▶ Residual Stromal Bed

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Central Epithelial Edema

► Sattler's Veil (Central Epithelial Edema)

Central Island

► Steep Central Islands

Central Pachymetry

► Central Corneal Thickness

Central Retinal Artery Occlusion, Ocular Ischemic Syndrome

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Synonyms

CRAO

Definition

Sudden, complete, and painless loss of vision in one eye, due to obstruction of normal blood flow in the central retinal artery to the retina. When this obstruction occurs, there is no proper blood supply to the retinal layers, and the retina becomes opaque and edematous, particularly in the posterior pole where the nerve fiber and ganglion cell layers are thickest. The retina appears bright, except the area of the fovea, which will still appear as an orange-red spot, because of the thin retinal layer at this area, and the orange reflex from the intact choroidal vasculature beneath this thin retinal layer. This phenomenon of orange-red spot in the middle of bright, edematous retina is called a cherry-red spot.

Etiology

Several etiologies are associated with the occlusion of retinal artery:

1. Embolic event due to:
   (a) Carotid artery atherosclerosis or dissection
   (b) Cardiac valvular disease
   (c) Cardiac arrhythmia
   (d) Left ventricular hypertrophy and systemic hypertension
   (e) Thrombus after myocardial infarction
   (f) Benign and malignant tumors of the heart
   (g) Organic heart malformation as patent foramen ovale and subsequent venous originated embolus (lipid emboli from pancreatitis, deep vein thrombosis embolus, or intravenous drug use)
   (h) Iatrogentic event as carotid endarterectomy or radiologic studies (carotid or cerebral angiography, cardiac catheterization, lymphography, hysterosalpingography)
2. Trauma due to retrobulbar injection, orbital floor fracture repair, or nasal surgery and penetrating injury
3. Coagulopathies:
   (a) Sickle cell disease
   (b) Genetic mutations of factors in a coagulation cascade (factor V Leiden, protein

C deficiency, protein S deficiency, antithrombin III deficiency, activated protein C resistance)
   (c) Lupus anticoagulant
   (d) Homocystinuria
   (e) Pregnancy or oral contraceptives use
   (f) Platelet abnormalities
   (g) Leukemia or lymphoma
4. Collagen vascular disease (giant cell arteritis, systemic lupus erythematosus, polyarteritis nodosa, Wegener's granolomatosis) and other vasculitis and inflammatory conditions (mucormycosis, toxoplasmosis, *Toxocara canis*, Lyme, Behcet, and cat scratch disease)
5. Ocular conditions as increased intraocular pressure (due to intravitreal injection, gas expansion after vitrectomy, prone intraoperative positioning, retrobulbar hemorrhage, orbital emphysema), optic neuritis, optic disk drusen, and peripapillary arterial loops

Embolization is the most important non-arteritic cause of CRAO, embolus from carotid artery atherosclerosis being the most common one. In patients younger than 40 years old, carotid disease is relatively rare. In these patients, cardiac embolism is the most common etiology.

Cholesterol emboli, which are also called Hollenhorst plaques, stand for 74% of all retinal artery emboli cases. They are seen typically at retinal arterial bifurcations as bright-yellow-colored plaques. These emboli usually suggest a carotid atheromatous origin, but they can also arise from the aortic arch, ophthalmic artery, or proximal central retinal artery. It is worth to note that the presence of a Hollenhorst plaque in the retinal artery occlusion is associated with a low prevalence of carotid atherosclerosis requiring carotid endarterectomy. Furthermore, in contrast to amaurosis fugax, such ocular findings are not associated with a high risk for hemispheric neurological events. However, patients with retinal emboli do have an associated higher mortality rate.

Calcific emboli that account for 15.5% of emboli are typically larger and cause more severe obstruction. They most commonly originate from the cardiac valves.

Another important cause of CRAO is an atherosclerosis-related thrombosis occurring at the level of the lamina cribrosa.

Systemic etiologic considerations, as coagulation disorders, sickle cell disease, infectious diseases, valvular and anatomical malformations of the heart, and arrhythmias, are important and require evaluation.

It is important to note that the leading cause of death in patients with retinal arterial obstruction is cardiovascular disease.

Connective tissue disorders as giant cell arteritis account for approximately 1–2% of cases of CRAO.

Clinical Presentation

The patient may complain of sudden, painless, monocular, severe loss of vision, which occurs acutely (span of a few seconds). Sometimes prior episodes of amaurosis fugax may be reported, and they may suggest an embolic source of the CRAO. Some cases of giant cell arteritis-related CRAO may also be associated with amaurosis fugax. The risk of CRAO after amaurosis fugax is about 1% per year.

Visual acuity is counting fingers to light perception in about 80% of cases. Some patients have a preserved central visual field thanks to a sufficient cilioretinal circulation which supplies some or all of the papillomacular bundle. Visual acuity in CRAO associated to giant cell arteritis is usually better compared to that following an embolic event.

No light perception at presentation is very rare and raises suspicion of patient's concomitant choroidal circulation deficit. Ophthalmic artery occlusion has to be ruled out.

An afferent pupillary defect usually develops within seconds following obstruction of the central retinal artery, regardless of macular sparing. The anterior segment will be quiet in majority of cases, but in about 17% of cases, rubeosis iridis may be seen. If acute rubeosis iridis is present, ocular ischemia secondary to the presence of a concomitant carotid artery obstruction should be considered. On fundoscopy evaluation, the retina

appears pale, except the reddish fovea. No hemorrhages are seen. The presence of hemorrhages may suggest co-occurrence of CRAO with central retinal vein occlusion. Intra-arterial emboli are visible in 20–40% of eyes.

Most classic and earliest signs at presentation are a cherry-red spot (90%) and posterior pole retinal opacity or whitening (58%). Other important fundoscopic signs are optic nerve pallor (39%), retinal arterial attenuation (32%), and optic disk edema (22%). Most of the retinal findings will predominantly be located in the posterior pole, whereas at periphery, it will appear normal. The size of the cherry-red spot is variable and is dependent on the width of the foveola. The classic signs will gradually disappear with time. One month after the CRAO presentation, the cherry-red spot is seen in about 19% and the retinal opacification in 17% of affected patients. Pathologically, this evolution corresponds to resolution of initial acute ischemia-induced intracellular edema with subsequent loss of neuronal cells and the development of an acellular scar of the inner retinal cell layers.

In the acute phase of nonarteritic CRAO, the disk may be normal, hyperemic, edematous, and, rarely, pale.

The optic nerve is acutely edematous in nearly all cases of arteritic (e.g., giant cell arteritis) CRAO as a result of the associated anterior ischemic optic neuropathy that is typically observed in these patients. The pallor of the nerve is due to ischemic opacification of the surface of the nerve fiber layer, which is normally supplied by retinal circulation.

Later on in the course of CRAO, chronic changes may appear on the fundoscopic examination: optic atrophy, retinal arterial attenuation, cilioretinal collaterals, macular RPE changes, and cotton wool spots.

Diagnostics

Finding the proper etiology for CRAO is very important for the treatment strategy and for the prevention of CRAO in the fellow eye, stroke, or other comorbidities.

Blood evaluation: complete blood count, biochemistry and coagulation analysis may yield some information about inflammation, infection, or clotting pathology. A hypercoagulability evaluation should be especially considered for patients younger than 50 years with a suggestive history of prior thrombosis or miscarriage or family history of coagulopathies.

Work-up includes blood tests for factor V Leiden mutation, protein C, protein S, and antithrombin III deficiencies, homocysteine levels, sickle cell disease, and lupus anticoagulant (LAC). Further evaluation of collagen vascular diseases (as antinuclear antibodies, C-ANCA, P-ANCA) may reveal an inflammatory etiology. Other tests for monoclonal gammopathy, cancer, infection, and disseminated intravascular coagulation may be ordered depending on the clinical circumstance.

Carotid Doppler imaging is important to establish the carotid artery origin of the emboli. Most retinal emboli are relatively small. From the ophthalmic point of view, when evaluating the results of carotid Doppler ultrasonography, the presence or absence of plaque is more important than whether a hemodynamically significant stenosis is present. The latter is more important in determining the need for carotid endarterectomy. Carotid Doppler also has its limitations, including the lack of imaging of the thoracic and intracranial portion of the carotid artery and poor resolution for detection of microemboli.

Electrocardiogram (ECG) and Holter ECG are indicated when heart arrhythmia is suspected. Furthermore, a baseline ECG is recommended for almost each patient, since the cardiac morbidity and mortality are significant in patients with retinal artery occlusion.

For heart malformation, valvulopathies, and infectious endocarditis, transthoracic or transesophageal echo is helpful for diagnosis. Transthoracic echo is less sensitive and thus will be performed in patients with low cardioembolic risk. Transesophageal echo is an important diagnostic tool for patients with high cardioembolic risk factors or for patients with suspicious clinical or transthoracic echo findings. A computed tomography angiogram (CTA) or magnetic

resonance imaging angiogram (MRA) should be considered in special cases such as suspected carotid or aortic dissection.

In cases of CRAO in which emboli are not readily visible, giant cell arteritis has to be suspected. For further diagnosis erythrocyte sedimentation rate (ESR) and blood test for C-reactive protein levels, should be obtained. These two tests (if elevated) improve the sensitivity and specificity for giant cell arteritis diagnosis. These two tests improve the sensitivity and specificity for giant cell arteritis diagnosis. Other acute phase reactant markers such as elevated platelet counts are also suggestive of giant cell arteritis. The definitive diagnosis is made with a temporal artery biopsy (although false-negative biopsy results are common).

Autofluorescence (AF)

In the acute phase, the area supplied by an occluded retinal artery shows decreased autofluorescence due to blockage of the normal autofluorescence of the RPE by the thickened inner retina. This blockage resolves over time and may evolve into a window defect with increased autofluorescence in the chronic phase as areas of significant inner retinal thinning develop.

Fluorescein Angiography (FA)

Variable residual retinal circulation is almost always seen in CRAO, but the arterial filling is delayed by 5–20 s and is slower than in normal arteries. Complete absence of retinal filling is rare. The fluorescein dye lines the arterial walls in a pattern similar to the laminar flow filling of normal retinal veins. When intra-arterial emboli are visible, the arteriovenous transit time can be even further delayed. There is a correlation between the severity of arterial obstruction and the initial visual acuity. Staining of the optic disk can be variable.

About 11% of patients may present also with areas of delayed choroidal perfusion. Leakage of fluorescein dye at the level of the RPE is generally not seen in CRAO, unless the choroidal circulation is involved.

In the chronic phase of CRAO, when the retinal circulation is reestablished, the FA may return to an almost normal appearance, but the damage to the infracted retina is irreversible. Therefore, vision loss, optic nerve atrophy, and arterial narrowing will persist.

Normalized FA and normal appearance of the optic nerve may suggest that the reperfusion took place before the irreversible damage has occurred. These cases have much better prognosis.

Optical Coherence Tomography (OCT)

In the acute stage, the macular contour is irregular. There is a hyperreflectivity of inner retinal layers that corresponds to intracellular edema and explains the lack of intraretinal and hyporeflective fluid spaces. Reflectivity of the outer retinal layers and RPE is blocked by the highly reflective inner retinal layer. There is no retinal thickening. At chronic stage, thinning and atrophy of the inner retina is shown, whereas an outer layer is well preserved. Thus, the use of OCT in cases of chronic, not previously diagnosed CRAO with normal fundus features is very important for the definitive diagnosis.

Visual Field (VF)

Central scotoma is the most common defect observed on macular visual field testing followed by paracentral scotoma. Patients with cilioretinal supply to the papillomacular bundle show a preserved central island of vision corresponding to the area perfused by the cilioretinal artery. Peripheral constriction is the most common visual field deficit noted in these patients. Choroidal derived blood supply may perfuse a nasal part of retina; thus, some patients will show a preserved temporal island.

Visual field defects improve in approximately 28% of patients, remain stable in 57%, and worsen in 7%.

Electroretinography (ERG)

Attenuation of the b-wave is more severe than that of the a-wave because the inner retinal layers are more affected by the poor retinal artery perfusion than the outer. This produces a characteristic negative waveform with the scotopic white stimulus.

A significant attenuation of both the a-wave and b-wave suggests a poor perfusion of the choroidal vasculature as well. In this case, ophthalmic artery occlusion has to be suspected.

Differential Diagnosis

Ophthalmic artery occlusion
Optic nerve ischemia

Prophylaxis

Anticoagulants are important for secondary prevention of cerebral and ocular infarction in patients with atrial fibrillation, acute internal carotid artery dissection, or a hypercoagulable condition. Their use for treatment of acute CRAO is doubtful.

Therapy

Treatment options are limited, and their efficacy is uncertain. Treatment should be started within a maximum 24 h of symptoms onset. Treatment strategy consists of dislodging emboli, reducing intraocular pressure and increasing retinal blood flow, vasodilating the ocular blood supply, improving retinal circulation, decreasing retinal edema, maintaining retinal oxygenation until spontaneous reperfusion, and acting on the thrombus.

Lowering the pressure may dislodge the embolus to further smaller division of the retinal artery and thus cause ischemic damage to smaller area of retina. The pressure may be reduced by performing an ocular massage, anterior chamber paracentesis, or use of retrobulbar anesthesia.

A mixture of 95% oxygen and 5% carbon dioxide (carbogen) can be provided to induce vasodilation and improve oxygenation, but efficacy has not been proven. Hyperbaric oxygen provides oxygen at levels of atmospheric pressure. The purpose of hyperbaric oxygen is to preserve the retina in an oxygenated state until recanalization and reperfusion occur, typically at 72 h. The hyperbaric oxygen increases the arterial oxygen pressure and thereby increases nitric oxide synthesis, leading to vasodilation. Case reports of successful treatment have been published, but currently treatment for ocular diseases is an off-label use of hyperbaric oxygen.

Vasodilating medications as pentoxifylline, nitroglycerin, and isosorbide dinitrate that may increase retinal blood flow have been suggested, but their efficacy has never been proven as was isovolemic hemodilution. If giant cell arteritis is suspected as a cause, corticosteroid therapy should be promptly instituted because the second eye can become involved by ischemia within hours to days after the first.

Experimental data have shown that retinal damage may arise not only from the presence of retinal nonperfusion but also from a cascade of events that injure cells after the tissue becomes reperfused. In the future, it may be possible to minimize damage with drugs that block this cascade of oxidative and membrane damage.

Iris neovascularization develops after acute CRAO in approximately 18% of eyes 1–12 weeks (average interval of 4–5 weeks) after the event. Full-scatter laser panretinal photocoagulation (PRP) causes successful regression in approximately 65% of cases.

Prognosis

With time, the central retinal artery may reopen or recanalize, and the retinal edema clears. However, the infarct to the retina usually causes an irreversible damage to the nerve cells; thus, the effect on visual acuity is usually permanent.

Visual acuity tends only to improve within the first week of onset with minimal chance for subsequent significant improvement. Visual recovery after treatment has been shown to correlate with presenting visual acuity and the duration of visual impairment. Although visual acuity may

spontaneously improve in up to 22% of patients with nonarteritic CRAO, less than 10% of patients report a meaningful recovery of vision.

About 66% of the eyes will have final vision worse than 20/400, and only in 18% the visual acuity will be of 20/40 or better. Most cases of 20/40 or better vision occur in the presence of a patent cilioretinal artery, which preserves the central macula. In most cases, the irreversible damage to the sensory retina occurs after 90 min of complete CRAO. Nevertheless, clinical return of vision can be seen in some instances, even if the obstruction has persisted for many hours.

Concomitant rubeosis iridis may occur in the setting of chronic CRAO. The risk of developing iris neovascularization is greater for obstruction lasting more than 1 week compared to those lasting only a few days.

Epidemiology

The estimated incidence of CRAO in general population is about 8.5/100,000. More than 90% of patients are older than 40 years, and the average age is early 60s. It is more common in males than in females. About 1–2% of cases are bilateral.

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Central Retinal Vein, Occlusion of

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Synonyms

CRVO

Definition

Blockage of the main vein of the retina (central retinal vein) that can result in macular edema, retinal ischemia, and ocular neovascularization (Figs. 1 and 2).

Etiology

The pathophysiology of CRVO is poorly understood but likely involves hemodynamic alterations resulting in stagnant flow and thrombus formation in the lumen of the central retinal vein. Concurrent systemic vascular disease, most commonly hypertension but including hyperlipidemia, arteriosclerosis, smoking, and diabetes mellitus, is the largest risk factor for CRVO.

Hypercoagulable states and inflammatory conditions may be present in persons with CRVO, particularly if less than 60 years of age. An increased incidence of coagulation cascade abnormalities, including protein C deficiency, protein S deficiency, activated protein C resistance, presence of factor V Leiden, presence of antiphospholipid antibodies, hyperhomocysteinemia, antithrombin III deficiency, prothrombin gene mutations, and abnormal fibrinogen levels, along with hyperviscosity from blood dyscrasias, dysproteinemias, and dehydration, among others, have also been reported with CRVO.

Open-angle glaucoma increases the risk of CRVO. External compression of the globe and optic nerve from thyroid-related ophthalmopathy, mass lesions, or head trauma with orbital fracture may also result in CRVO.

CRVO may result in vision loss through secondary macular edema and neovascularization, which are modulated by growth factors released from the ischemic retina, including vascular endothelial growth factor (VEGF), interleukins (IL) such as IL-6, IL-8, IP-10, MCP-1, and PDGF-AA. Intraocular VEGF levels correlate with severity of macular edema and neovascularization, and VEGF suppression has emerged as the mainstay of CRVO treatment.

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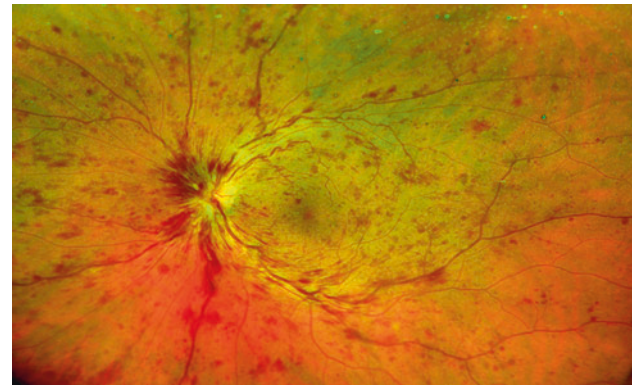
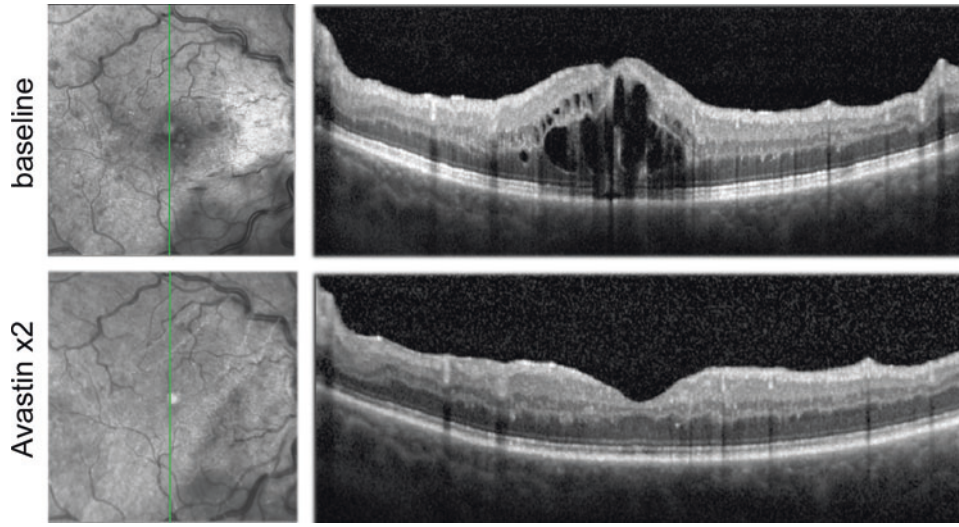


Fig. 1 Classic findings of CRVO include a "blood and thunder appearance" with 360° retinal hemorrhages, venous tortuosity, and macular edema



Central Retinal Vein, Occlusion of, Fig. 2 CRVO-associated macular edema at baseline is resolved following intravitreal anti-VEGF pharmacotherapy

Clinical Presentation

Central retinal vein occlusion usually presents with sudden painless loss of vision in one eye. On examination, the retinal venous system is typically engorged and tortuous with superficial nerve fiber layer and intraretinal hemorrhages in all four quadrants. These hemorrhages radiate from the optic nerve head, are variable in quantity, and may result in the classic "blood and thunder" fundus appearance. Optic nerve head swelling, cotton-wool spots, macular edema, and, less commonly, a cilioretinal artery occlusion may also be present.

The extent of retinal hemorrhage may decrease or resolve completely. Persistent macular edema may result in variable degrees of secondary retinal pigment epithelium alterations. Epiretinal membrane formation can also occur. Optociliary shunt vessels, which are collateral vessels to the choroidal vascular system, can develop on the optic nerve head.

In the absence of treatment, macular edema often chronically persists despite resolution of retinal hemorrhages. Neovascularization of the optic disc (NVD), retinal neovascularization elsewhere (NVE), and anterior segment neovascularization

of the iris (NVI) and/or neovascularization of the angle (NVA) may develop as a response to secondary retinal ischemia and may lead to vitreous hemorrhage, tractional retinal detachment, and/or neovascular glaucoma (often within the first 3 months, referred to as "90-day glaucoma"), respectively.

Diagnostics

For the majority of CRVO patients, who are over 65 years of age and have systemic vascular risk factors, a laboratory workup is typically not necessary. The blood pressure may be checked in the ophthalmologist's office, and the patient is referred to his/her internist for timely systemic evaluation and management of vascular risk factors. In persons less than 65 years of age and particularly in younger patients without systemic vascular risk factors, a hypercoagulable workup (protein C, protein S, factor V Leiden, antiphospholipid antibodies, homocysteine, antithrombin III, prothrombin, and fibrinogen) should also be considered.

Differential Diagnosis

The clinical findings in eyes with a CRVO are often pathognomonic but may occasionally be similar to findings seen in diabetic retinopathy, hypertensive retinopathy, ocular ischemic syndrome, radiation retinopathy, and leukemic retinopathy.

The differential diagnoses for underlying factors associated with CRVO include:

- Systemic vascular diseases: hypertension, carotid insufficiency, diabetes mellitus, prior radiation to the head
- Ocular diseases: open-angle glaucoma, ischemic optic neuropathy, pseudotumor cerebri, tilted optic nerve head, optic nerve head drusen
- Hematologic alterations: hyperviscosity syndromes such as dysproteinemias (multiple myeloma), blood dyscrasias (polycythemia vera, lymphoma, leukemia, sickle cell disease or trait), anemia, hypercoagulable states (factor V Leiden, elevated plasma homocysteine, elevated fibrinogen, factor XII deficiency, antithrombin III deficiency, antiphospholipid antibody syndrome, activated protein C resistance, protein C deficiency, protein S deficiency)
- Inflammatory/autoimmune vasculitis: systemic lupus erythematosus
- Medications: oral contraceptives, diuretics, hepatitis B vaccine
- Infectious vasculitis: HIV, syphilis, herpes zoster, sarcoidosis
- Other: dehydration, pregnancy, retrobulbar block

Prophylaxis

Timely identification and treatment of systemic vascular risk factors, such as systemic hypertension and diabetes mellitus, is important in individuals with CRVO. Systemic anticoagulation, such as with aspirin or warfarin, has not been shown to prevent or alter the natural history of CRVO. The prophylactic use of these medications may help prevent non-ocular thrombotic events, especially in individuals with known systemic vascular disease, and their use may be considered in coordination with the patient's internist.

Therapy

Most current treatments for CRVO are directed not toward the underlying thrombus but rather the treatable sequelae of CRVO, particularly macular edema and neovascularization. First-line therapy for CRVO-associated macular edema typically consists of intravitreal administration of anti-VEGF agents or corticosteroids. Anti-VEGF agents used to treat CRVO include ranibizumab 0.5 mg (Lucentis, Genentech, Inc., San Francisco, CA, monthly injections with 14.9 letter mean improvement versus 0.8 letter mean improvement with sham monthly injections after 6 months in the ranibizumab for the treatment of macular edema after Central Retinal Vein Occlusion Study: Evaluation of Efficacy and Safety (CRUISE) trial)

(Brown et al. 2010), aflibercept 2 mg (Eylea, Regeneron, Inc., Tarrytown, NY, monthly injections with 17.3 letter improvement versus 4.0 letter loss with sham monthly injections after 6 months in the Controlled Phase 3 Evaluation of Repeated Intravitreal Administration of VEGF Trap-Eye in Central Retinal Vein Occlusion: Utility and Safety (COPERNICUS) trial Boyer et al. (2012) with equivalent results in the parallel General Assessment Limiting Infiltration of Exudates in Central Retinal Vein Occlusion with VEGF Trap-Eye (GALILEO) study), and bevacizumab 1.25 mg (Avastin, Genentech, Inc., used off-label for treatment of retinal diseases).

Corticosteroids used for treatment of CRVO include a sustained release dexamethasone implant 0.7 mg (Ozurdex, Allergan, Inc., Irvine, CA – single injection with 29% rate of >15 letter gain at day 60 versus 9% with single sham injection in the post hoc analysis of the CRVO subgroup of the Global Evaluation of Implantable Dexamethasone in Retinal Vein Occlusion with Macular Edema (GENEVA) trial) (Haller et al. 2010) and triamcinolone acetate 1 mg (q4 month injections with −1.2 letter mean loss (26% with >15 letter gain) versus −12.1 letter loss (7% with >15 letter gain) with observation in Standard Care versus Corticosteroid for Retinal Vein Occlusion (SCORE)-CRVO trial).

Without data from large trials directly comparing the efficacies of these intravitreal agents, it is not clear if any agent is superior to the other. Because of the side effects, particularly cataract and elevated intraocular pressure, associated with corticosteroid administration, anti-VEGF agents are typically used first-line. In contrast to branch retinal vein occlusions, grid-pattern argon laser photocoagulation was found to reduce macular edema but not improve visual acuity in the Central Retinal Vein Occlusion Study (CVOS) and is therefore not recommended in treatment of CRVO-associated macular edema.

Treatment of CRVO-associated ocular neovascularization consists of panretinal laser photocoagulation (PRP). The CVOS examined optimal timing of PRP treatment. Prophylactic PRP did not significantly decrease the onset of neovascularization and resulted in decreased efficacy of subsequent PRP placement, so the CVOS recommended prompt, but not prophylactic, PRP placement upon development of anterior segment neovascularization. While the use of anti-VEGF therapy may be useful in inducing rapid regression of neovascularization, such therapy is a temporizing adjunct that should be administered in conjunction with PRP treatment if ocular neovascularization is present.

Prior to the development of intravitreal pharmacotherapy for CRVO, various alternative treatments were explored in the absence of robust therapies, including tissue plasminogen activator administration through either a systemic, intravitreal, or direct retinal vein cannulation approach; pars plana vitrectomy with or without internal limiting membrane peeling; laser or surgical chorioretinal anastomosis creation; and radial optic neurotomy. While successes with each approach have been reported, these results have not been consistently reproducible and have been associated with a significant complication profile. These approaches have largely been abandoned since the development of intravitreal pharmacotherapy.

Prognosis

The natural history of CRVO was followed in the Central Vein Occlusion Study. An important prognostic indicator of final visual outcome was visual acuity at the time of presentation. Baseline visual acuity was 20/40 or better in 29% of affected eyes, 20/50–20/200 in 43%, and 20/250 or worse in 28%; median baseline acuity was 20/80. The majority of those with initial visual acuity of 20/40 or better maintained this acuity. Individuals with intermediate visual acuity (20/50–20/200) had a variable outcome: 21% improved to better than 20/50, 41% stayed in the intermediate group, and 38% were worse than 20/200. Persons with poor visual acuity at presentation (less than 20/200) had only a 20% chance of improvement. The development of intravitreal pharmacotherapy for CRVO has provided significant improvements beyond the natural history of disease with a more favorable prognosis for visual rehabilitation.

Epidemiology

Retinal vein occlusions (both central and branch, including hemi) are the second leading cause of vision loss from retinal vascular dysfunction, behind diabetic retinopathy. CRVO accounts for approximately 25% of retinal vein occlusions. Prevalence of CRVO is estimated at <0.1–0.4%, affecting men and women equally and occurring predominantly in persons over the age of 65 years with coexisting systemic vascular comorbidities. CRVO is typically unilateral, but the annual risk of retinal vascular occlusion in the fellow eye is approximately 1% per year, and up to 7% of patients with CRVO may develop CRVO in the fellow eye within 5 years.

Cross-References

► Optic Disc in Central Retinal Vein Occlusion

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Central Serous Chorioretinopathy/ Choroidopathy

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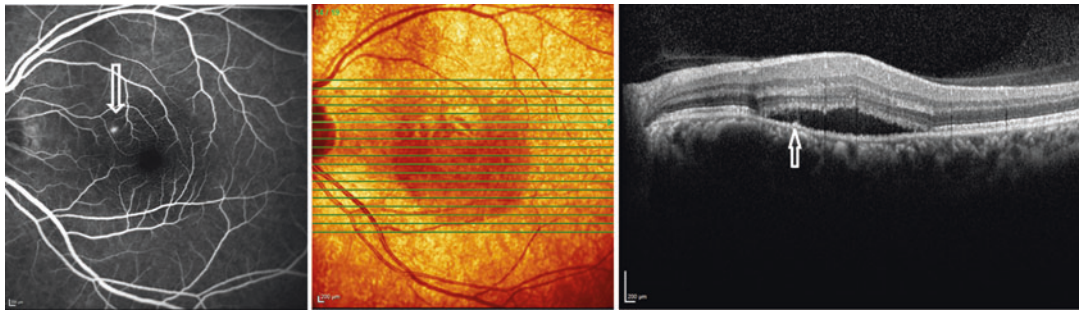
Synonyms

Central angiospastic retinopathy; Diffuse retinal pigment epitheliopathy; Idiopathic central serous retinopathy/chorioretinopathy

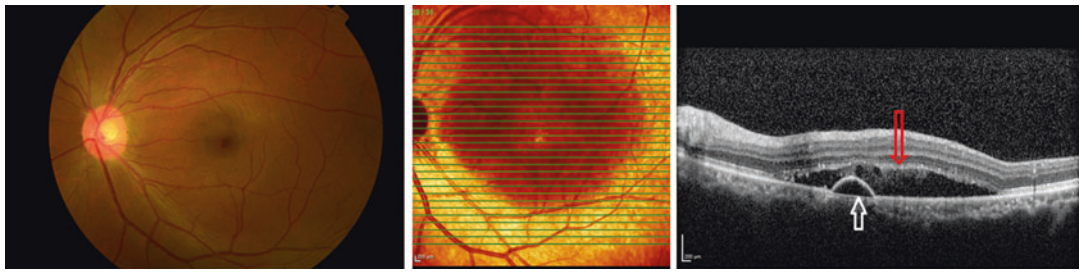
Definition, Pathogenesis, and Etiology

Central serous chorioretinopathy (CSC) is characterized by a serous detachment of the neurosensory retina that usually affects the macula and the posterior pole (Fig. 1). On fundus fluorescein angiogram (FFA), there is a classic "smokestack" or "ink blot" pattern of choroidal leakage in a proportion of patients. CSC commonly affects young men aged between 30 and 50 years of age. The prevalence of CSC is 9.9 cases per 100,000 in men and 1.7 cases per 100,000 in women.

The pathophysiology of CSC is unknown and has been thought to involve multiple mechanisms such as stasis and ischemia affecting the choroidal circulation (Nicholson et al. 2013). It has been hypothesized that a hyper-dynamic and hyper-permeable choroid causes increased hydrostatic pressure in the choroidal vessels. This leads to both the formation of pigment epithelial detachments (PEDs) (Fig. 2) and the breakdown of the retina pigment epithelium (RPE) barrier causing the leakage of fluid through the RPE cell tight junctions into the subretinal space, leading to the



Central Serous Chorioretinopathy/Choroidopathy, Fig. 1 Spectral domain OCT image (*right*) showing a CSC with an underlying RPE breakdown which corresponds to the area of leakage on FFA (*white arrow*)



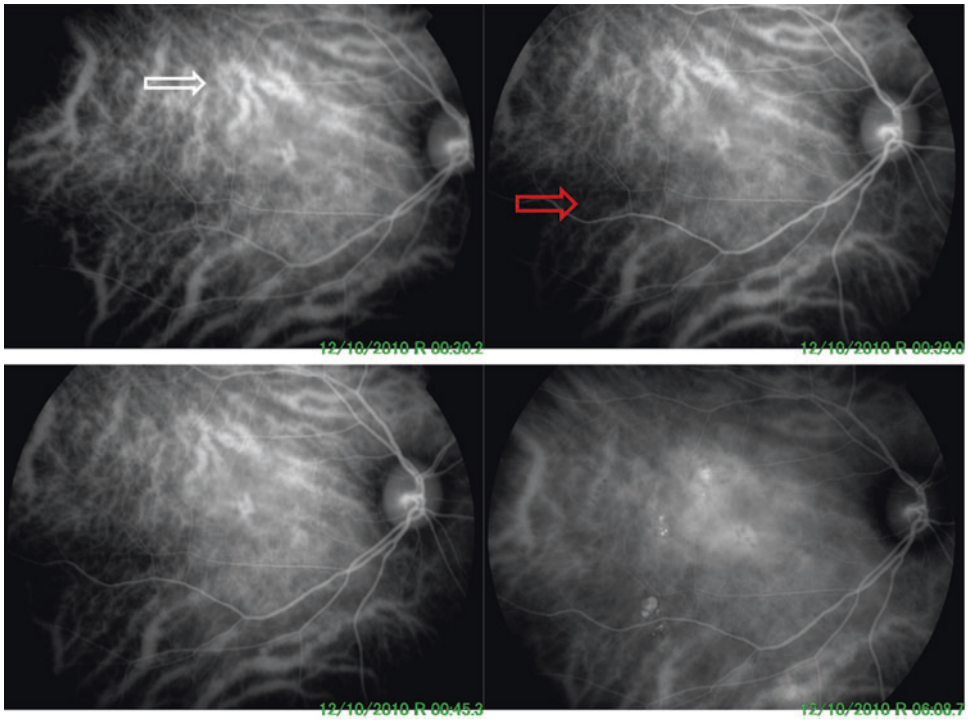
Central Serous Chorioretinopathy/Choroidopathy, Fig. 2 Fundus photo showing *white-gray* discoloration of the fovea due to fibrin deposition and cloudy subretinal fluid. The corresponding spectral domain OCT image (*right*) showing a CSC with an underlying PED (*white arrow*) and hyper-reflective material within the subretinal space due to fibrin deposition (*red arrow*)

classic serous detachment of neurosensory retina seen (Fig. 1) (Ryan 2012).

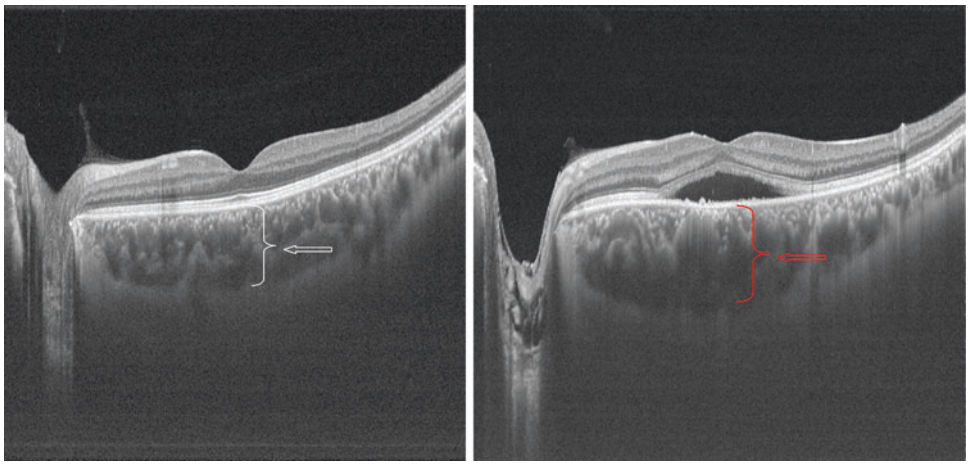
Animal models of CSC have shown damage to the endothelium of the choriocapillaries and fibrin clots, with leakage of fibrin into Bruch's membrane. Newer studies have also shown increased serum plasminogen activator inhibitor-1 (a fibrinolysis inhibitor) levels in patients with CSC, and this may support an underlying thrombotic mechanism. Another study with aqueous samples showed lower levels of the platelet-derived growth factor (PDGF) in the eyes with CSC than controls, suggesting that abnormal coagulation and platelet aggregation may also be involved in the pathogenesis of CSC (Nicholson et al. 2013).

Indocyanine green angiography (ICG) has shown supporting evidence of choroidal hyper-permeability with increased hyper-fluorescence of the choroidal vessels and areas of choriocapillary non-perfusion corresponding to focal areas of hypo-fluorescence (Fig. 3) (Ryan 2012; Nicholson et al. 2013). Optical coherence tomography (OCT) with enhanced depth imaging (EDI) in patients with CSC has shown a thickened choroid in both the affected and contralateral eyes (Fig. 4). Fibrin deposition in CSC lesions can also be observed clinically and on OCT imaging in humans (Fig. 2) (Agarwal 2012).

For the majority of case, the primary etiology is unknown. However, some secondary etiological agents have been described. Corticosteroids, both exogenous and endogenous, have been strongly associated with the development of CSC. The elevated levels of these compounds activate adrenergic receptors in the sympathetic nervous system and are thought to impair the auto-regulation of the choroidal vasculature (Nicholson et al. 2013). Early reports, which linked exogenous corticosteroid use to the incidence of CSC, include systemic steroids used for the treatment of autoimmune diseases or immunosuppression



Central Serous Chorioretinopathy/Choroidopathy, Fig. 3 ICG images showing areas of hyper-fluorescence (*white arrow*) consistent with choroidal hyper-permeability and areas of hypo-fluorescence (*red arrow*) consistent with areas of choriocapillary non-perfusion



Central Serous Chorioretinopathy/Choroidopathy, Fig. 4 Enhanced depth imaging OCT showing a thickened choroid in both the eye affected with CSC (*red arrow*) and the contralateral unaffected eye (*white arrow*)

after organ transplantation. In addition, the use of topical, intranasal, intra-articular, intramuscular corticosteroids has been reported to be risk factors for CSC. Excessive endogenous steroids in diseases like Cushing's syndrome and pregnancy are also associated with CSC. A previous study has reported an association of CSC with the type A personality trait (Ryan 2012). Some other

studies have reported an association with psychosocial stressors, in addition to inadequate coping mechanisms and the onset of CSC. Some newer studies have shown that there are also significant mineralocorticoid receptors in the choroid and this may be involved in CSC pathogenesis.

CSC is also associated less commonly with other diseases, such as systemic lupus erythematosus, sarcoidosis, Crohn's disease, paraproteinemia, Goodpasture's syndrome, and thrombotic thrombocytopenic purpura (Agarwal 2012). However it is uncertain whether the disease itself or the subsequent treatment with corticosteroids causes CSC (Liew et al. 2013; Nicholson et al. 2013).

Smaller studies have shown weaker associations of CSC; for example, higher level of basal endogenous catecholamines is thought to explain why obstructive sleep apnea (OSA) is associated with CSC. In one report, the treatment of OSA with continuous positive airway pressure (CPAP) resulted in the rapid resolution of bilateral CSC. An association with *Helicobacter pylori (H. pylori)* infection and CSC has been reported in recent studies. Thrombotic disease is a possible pathogenesis of this association. In one study 40% of CSC patients had *H. pylori* infection versus 25% of controls ($p = 0.0036$). Apart from corticosteroid use, other medications like 5-phosphodiesterase inhibitors (e.g., sildenafil and tadalafil) have been associated with CSC. Some case reports have reported a resolution of CSC after cessation of these medications; however a larger case-control study failed to confirm such an association (Nicholson et al. 2013). Antibiotics, psychopharmacological medications, alcohol, hypertension, and allergic respiratory disease have all been reported in small studies as potential risk factors of CSC.

A genetic basis to the pathogenesis of CSC is still not well established. There are numerous reports of familial CSC, and one study found a 52% rate of CSC-like pathology in families of chronic CSC patients. Despite the clinical findings, only a small percentage reported CSC symptoms. Previous studies have performed analyses on aqueous samples of CSC eyes for various cytokines and growth factors. Vascular endothelial growth factor (VEGF) levels in the aqueous were not found to be elevated in CSC; however this was controversial, as secondary choroidal neovascularization (CNV) that can be a complication of CSC responds well to anti-VEGF therapy. PDGF levels were reported as lower than controls, and this could be a possible mechanism of RPE dysfunction. Other cytokines like IL-6, IL-8, and monocyte chemoattractant protein-1 were found at similar levels in both CSC and control groups (Nicholson et al. 2013).

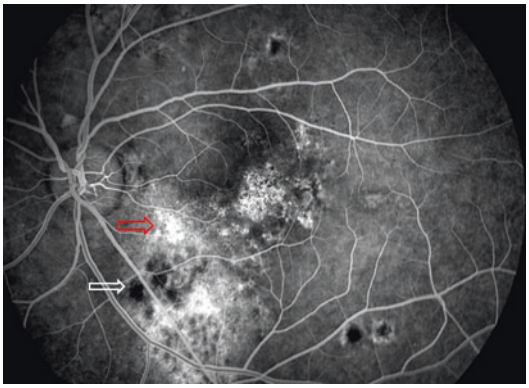
Clinical Presentation

Symptoms

The hallmark characteristics of CSC include blurring of vision, a relative central scotoma, metamorphopsia, and a hyperopic shift. In some patients, where the CSC does not involve the central macula area, they can be asymptomatic. Once the detachment reaches the central macula, it will cause distortion of the photoreceptor arrangement. In areas where there is crowding of the photoreceptors, the patient will experience macropsia; in other areas with a reduction in the number of photoreceptors per unit area, micropsia will result. Dyschromatopsia with a decrease in color saturation, contrast sensitivity, and a delay in retinal recovery time after exposure to light are other symptoms associated with CSC. A hyperopic shift occurs as the neurosensory retinal is pushed forward.

CSC can nominally be classified as acute and chronic; however the definition of the chronic form is not well defined and can range from 3 to 6 months of persistent fluid. Other studies have classified CSC based on the pathology at the level of the RPE. "Classic CSC" has pinpoint leaks at the RPE with minimal focal RPE changes (Fig. 1), while diffuse retinal pigment epitheliopathy (DRPE) has extensive RPE damage and diffuse leakage (Fig. 5) (Nicholson et al. 2013).

The initial episode of acute CSC tends to resolve without serious long-term sequelae. Recurrence of acute CSC, however, is common and has been reported in 15–50% of patients in previous studies. Thirty-three to 50% of CSC



Central Serous Chorioretinopathy/Choroidopathy, Fig. 5 FFA of a patient with chronic CSC showing areas of hypo-fluorescence corresponding to areas of RPE atrophy (*white arrow*) and areas of diffuse hyper-fluorescence consistent with diffuse leakage from the RPE (*red arrow*)

patients experience the first recurrence within the first year of follow-up, while 10% may have three or more recurrences up to 15 years after presentation. The initial presentation of this disease is usually unilateral, but bilateral involvement is reported to affect up to 40% of cases. Recent imaging studies have also documented subclinical structural changes in the contralateral eye of CSC patients (Fig. 4). Risk factors for bilateral involvement include chronic CSC and CSC associated with corticosteroids use (Ryan 2012; Liew et al. 2013).

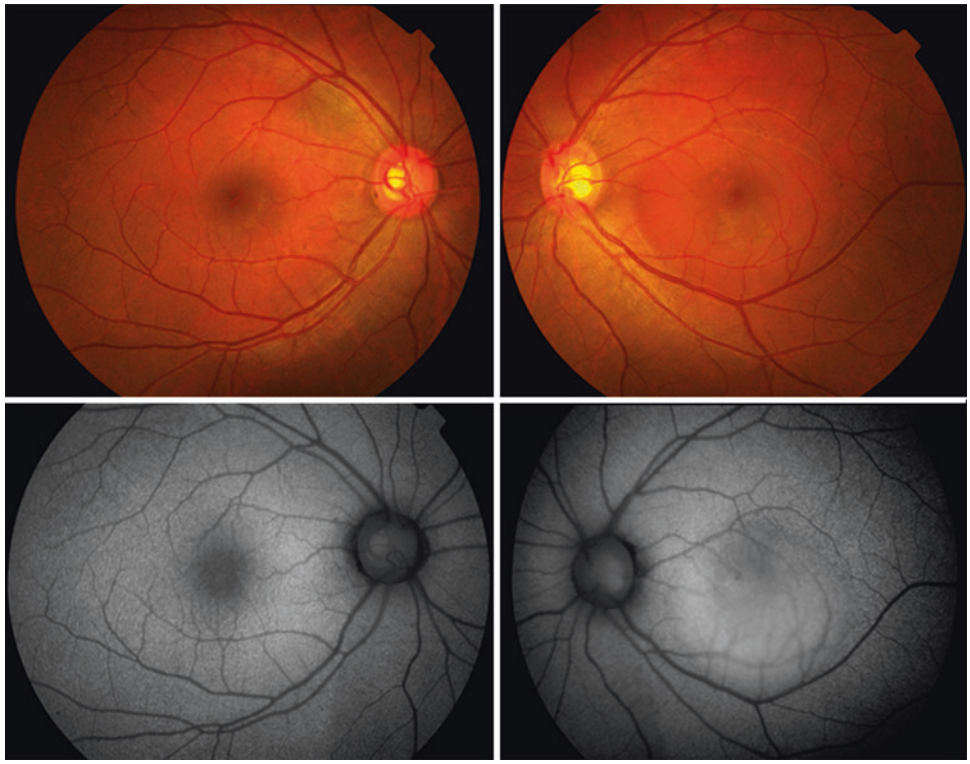
Signs

Clinical findings include a well-demarcated round or oval elevation of the neurosensory retinal, often involving the macula. The foveal reflex is decreased or absent, and the affected area often appears darker than the surrounding area as seen on slit-lamp biomicroscopy (Fig. 6). An associated PED may be present within or adjacent to the neurosensory detachment in 5–63% of all cases. This PED can be solitary or multiple and is typically small (Fig. 2). The areas between the detached and attached RPE appear as a well-circumscribed halo outlining the base of the lesion (Fig. 7). Yellow deposits on the underside of the detached retina are thought to arise from previous phagocytosis of photoreceptor outer segments after shedding. A yellowish discoloration of the foveal region is thought to arise from the increased visibility of the xanthophyll pigment (Fig. 6) (Agarwal 2012; Ryan 2012). The serous fluid within the detachment is mostly clear however in 10% of cases can be cloudy. In these cases, fibrin is deposited in the subretinal space forming a gray-white fibrinous lesion (Fig. 2), which can be misdiagnosed as focal retinitis, a cotton wool spot, or a subretinal neovascular membrane. Some patients develop a bullous serous retinal detachment as the subretinal fluid settles inferiorly (Fig. 8a). In chronic CSC cases, RPE atrophy on the retina can be seen connecting the macula to the inferior bullous detachment (Fig. 8b). The vitreous of a CSC patient is clear with no inflammatory cells.

Diagnostics (Imaging)

Optical Coherence Tomography (OCT)

Recent advances in new high-resolution imaging techniques have enabled better visualization of structures and understanding of the underlying pathophysiology of CSC. Spectral domain OCT (SDOCT) imaging, including enhanced depth imaging (Fig. 4), has enabled imaging of not only the retinal but the choroid. High-definition images of the central serous detachment, serous PEDs, and the underlying choroid have allowed detailed studies of these structures that were not possible using conventional slit biomicroscopy. The choroidal layer in CSC patients has been found to be thickened when compared to controls in both the affected and contralateral eyes (Fig. 4). This suggests a much greater incidence of subclinical bilateral involvement than previously reported. The underlying cause for the thickened choroid is not certain; however this is thought to be related to choroidal vasculature hyperpermeability as seen in ICG angiography (Fig. 3). Choroidal thickness on OCT is a useful parameter, which can be used to monitor disease progression and response to treatment. Visual acuity has been linked with the thickness of the outer nuclear layer (ONL) and the integrity of the inner segment ellipsoid zone (EZ). During chronic CSC, photoreceptor apoptosis and subsequent



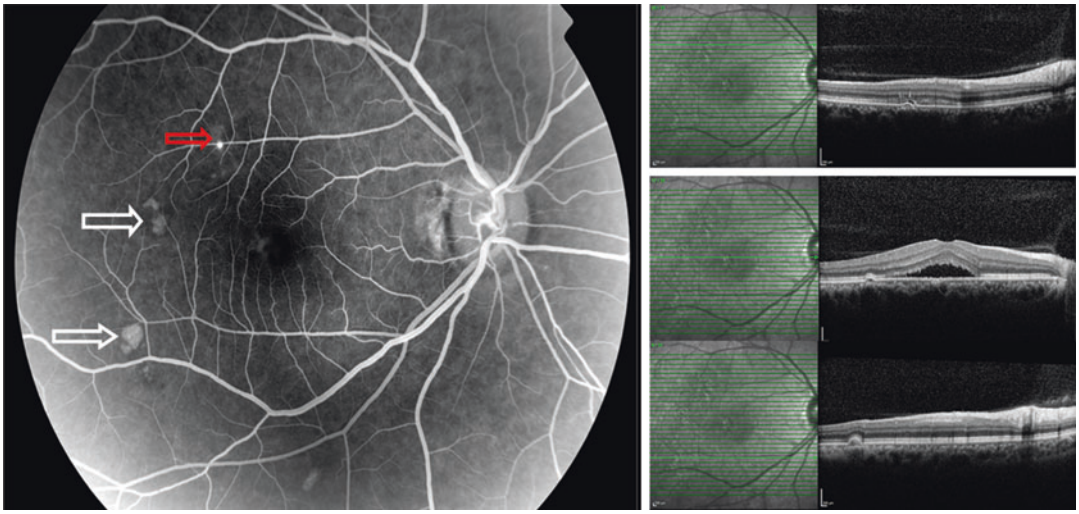
Central Serous Chorioretinopathy/Choroidopathy, Fig. 6 A fundus photo of a patient (*top right*) with CSC involving the macula, as demonstrated by a reduced foveal reflex and a slightly darker elevated region of the neurosensory detachment. The other contralateral eye (*top left*) is unaffected. FAF (*bottom right*) of the CSC shows blocked hypo-fluorescence at the fovea and a mild hyperfluorescent border around the neurosensory detachment more marked inferiorly

atrophy in the foveal region cause thinning of the ONL and disruption of the EZ layer and may result in poorer visual acuity (Fig. 9). In many cases, there is also a corresponding atrophic area of hypo-autofluorescence (AF) seen on autofluorescence (AF) imaging (Fig. 9).

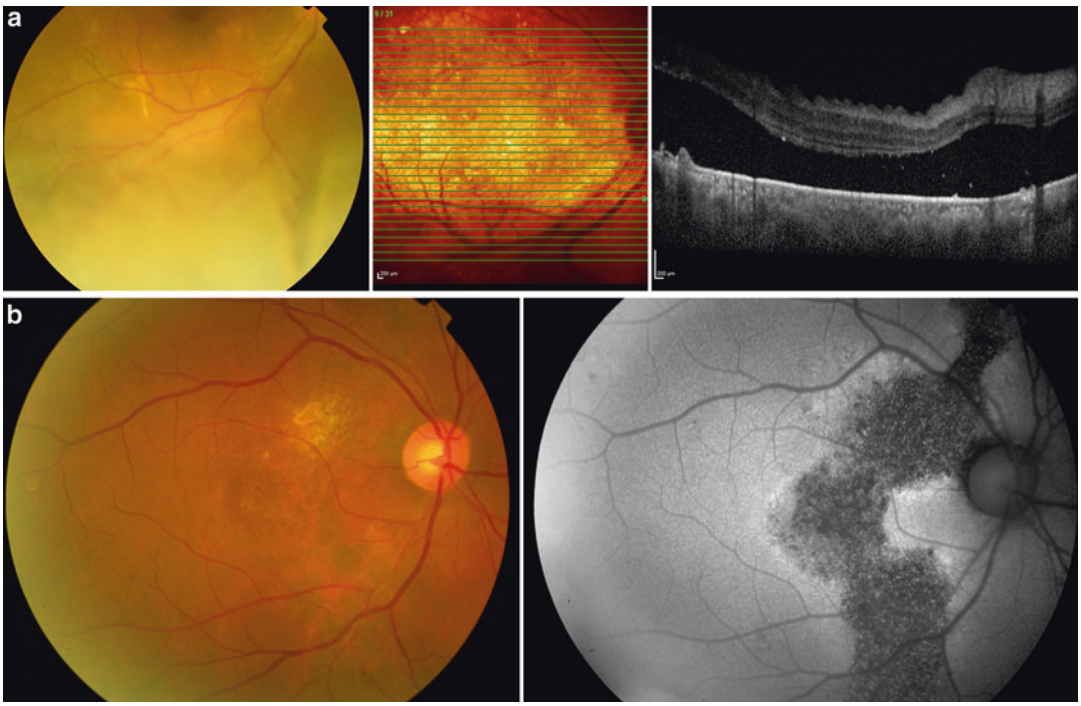
Punctate precipitates and yellow-white material have been observed in 65% of CSC patients and can be seen as hyper-reflective dots on the OCT image both within the retina and in the subretinal space (Figs. 10 and 11). This often correlates with clinical slit-lamp findings and fundus photography. The nature of these substances is still unclear, but possible hypothesis includes shed unphagocytosed photoreceptor outer segments and accumulations of fibrin, lipid, or macrophages clearing the subretinal space from debris (Liew et al. 2013; Nicholson et al. 2013). Focal areas of RPE breaches can be imaged on OCT, and this can correspond with leakage on FFA from the choroid (Fig. 1) (Nicholson et al. 2013). These areas adjacent to the leak on FFA frequently are sites for PED formation. Intraretinal cysts and subretinal fibrosis seen on OCT are also more common in chronic CSC and have a poorer visual prognosis (Liew et al. 2013).

Fundus Fluorescein Angiography (FFA)

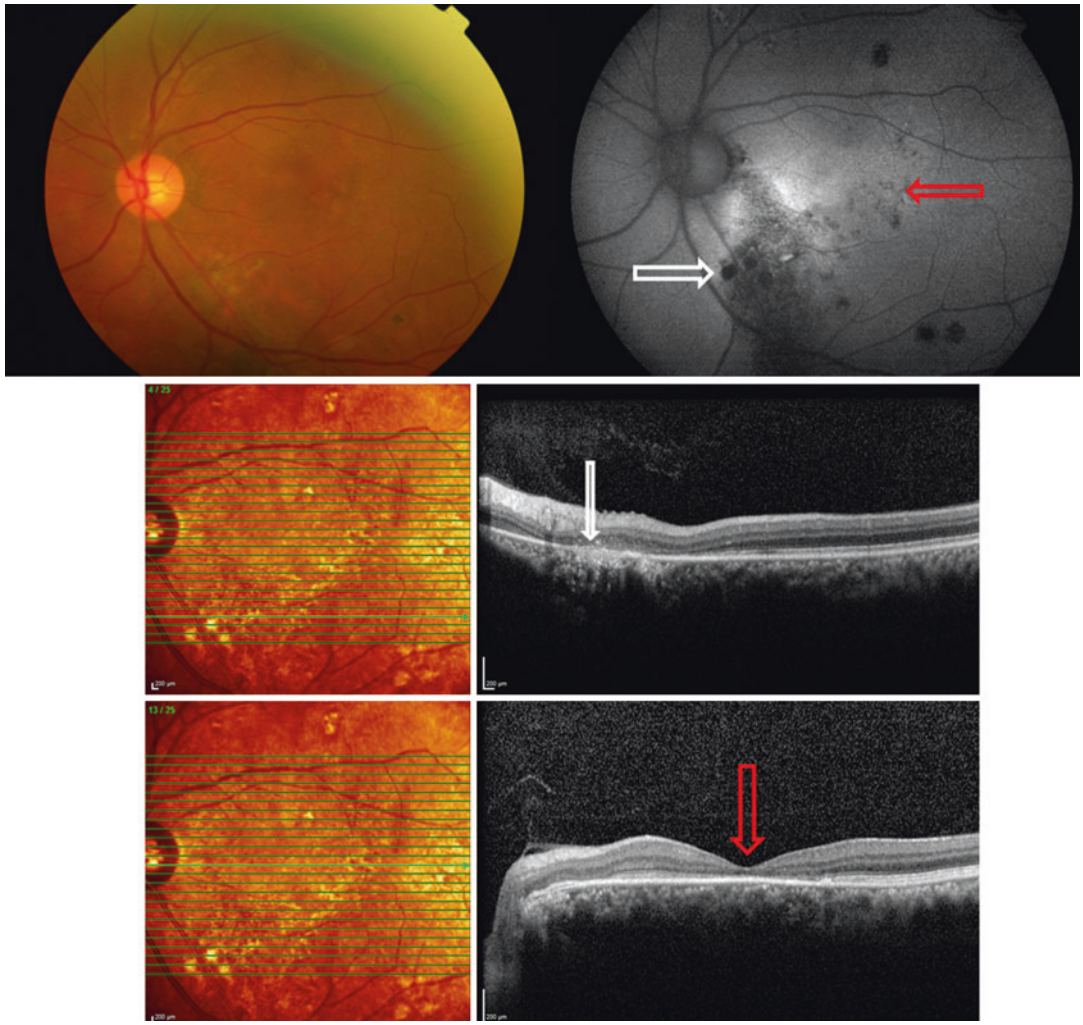
In acute CSC, two distinct patterns of FFA leakage have been described: ink blot or smokestack. The ink blot pattern is caused initially by the fluorescein leaking from the fenestrated choriocapillaries across Bruch's membrane staining the fluid in the sub-RPE space. This round spot of hyperfluorescence enlarges concentrically to fill the area of the PED. In some patients the dye may



Central Serous Chorioretinopathy/Choroidopathy, Fig. 7 FFA (*left*) of a patient with CSR and multiple adjacent PEDs. The superior PED (*red arrow*) is located in the area of leakage causing the neurosensory detachment inferiorly. Corresponding OCT images showing cross sections of the PED is shown – red arrow (*corresponding to top right OCT images*) shows actively leaking PED and the white arrows (*corresponding to the middle right and bottom right OCT images*) show non-leaking PEDs



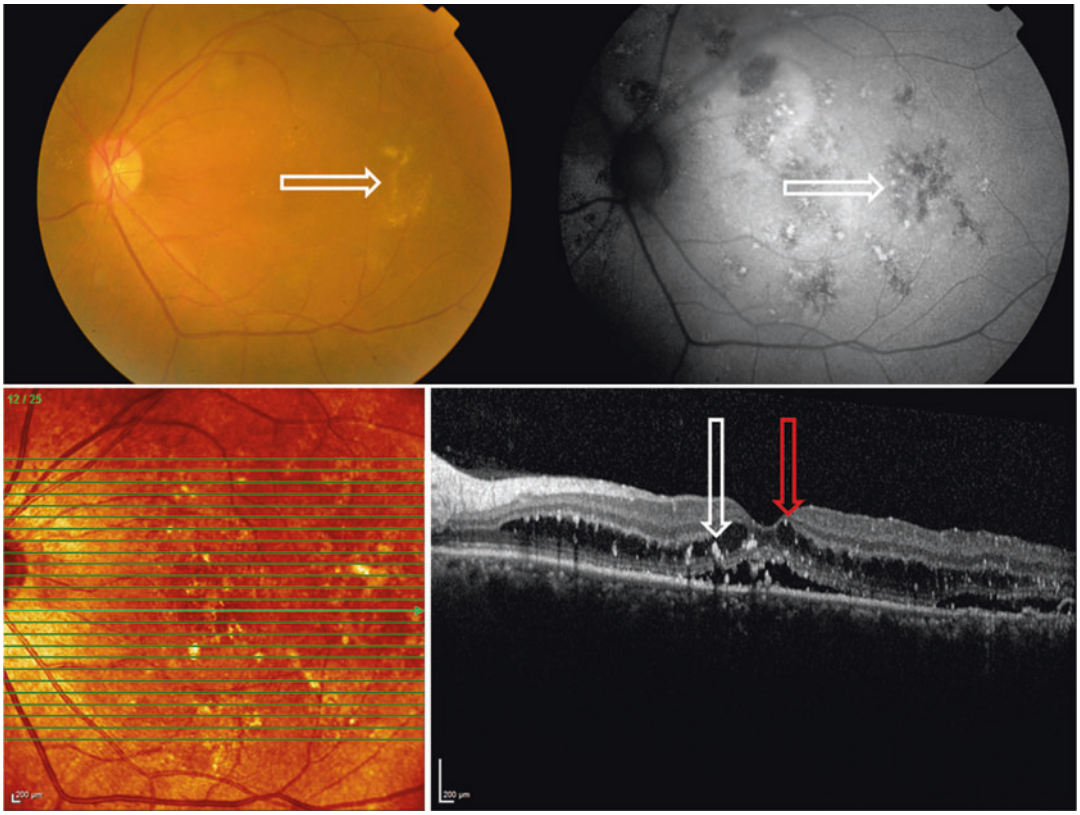
Central Serous Chorioretinopathy/Choroidopathy, Fig. 8 (**a**) Fundus photo (*left*) showing an inferior bullous retinal detachment from a multifocal chronic CSC and the corresponding OCT. (**b**) RPE atrophy tracts connecting the macula to the inferior bullous detachment as seen on color fundus photo (*left*) and hypoautofluorescent area on FAF (*right*)



Central Serous Chorioretinopathy/Choroidopathy, Fig. 9 A fundus photo (*left*) of a patient with resolved CSC showing areas of RPE atrophy corresponding to the areas of hypo-fluorescence on FAF (*right*). The corresponding OCT image shows disruption of the EZ line and thinning of ONL (*red* and *white arrow*). Granular hypo-fluorescence at the fovea region is consistent with a poor visual acuity of 6/90

be confined to the sub-RPE space but in other patients with the dye will diffuse into the subretinal space and cause the subretinal exudate surrounding the PED to be hyper-fluorescent (Fig. 12). The smokestack pattern has only been reported in 10% of cases. It is caused by the dye from the sub-RPE space leaking through a small pinpoint breach in the RPE at the inferior margin of the PED then flowing upward into the subretinal exudate in an umbrellalike or mushroomlike pattern (Fig. 13). It has been proposed that this pattern of leakage is due to the differential specific gravity of the dye and the subretinal exudates, causing convectional currents. In the late stages, all the subretinal exudates will be hyper-fluorescent, except in the foveal region, where it is blocked by luteal retinal pigment (Agarwal 2012; Ryan 2012).

In chronic, extensive CSC with PED and atrophy, RPE window defects may be observed. In multifocal CSC multiple areas of leakage may be observed, and FFA can help differentiate CSC from other inflammatory diseases or secondary choroidal neovascularization (Fig. 14; Agarwal 2012).



Central Serous Chorioretinopathy/Choroidopathy, Fig. 10 Fundus photo and FAF imaging which show yellow-white material, which is also seen as hyper-reflective dots on OCT within the retina and the subretinal space (*white arrows*). Intraretinal cysts and schisis changes (*red arrow*) that can be seen in chronic CSC

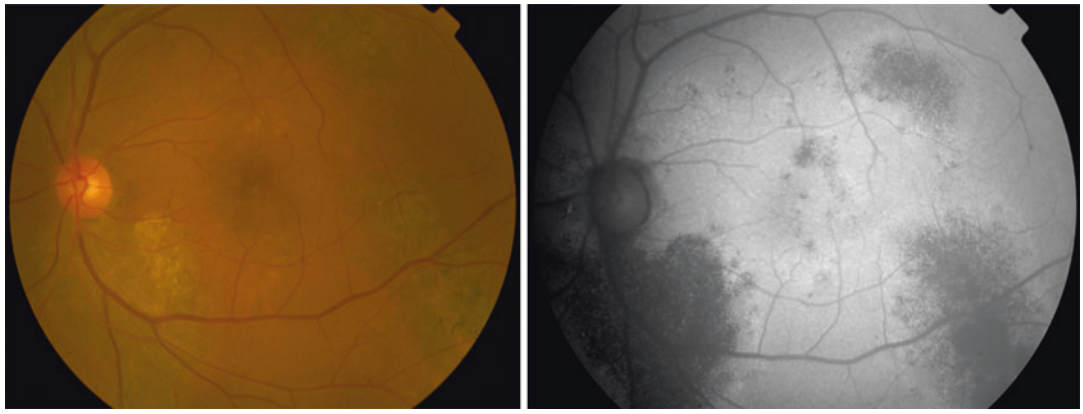
Most often the source of leakage is located in the posterior pole, one disc diameter away from the fovea. During FFA, attention should be focused on the more superior portion of the subretinal detachment as it is commonly the site of the leak due to gravity. About 30% of leakage occurs in the superior nasal quadrant, and 25% occurs in the papillomacular bundle (Agarwal 2012).

Indocyanine Green Angiography (ICG)

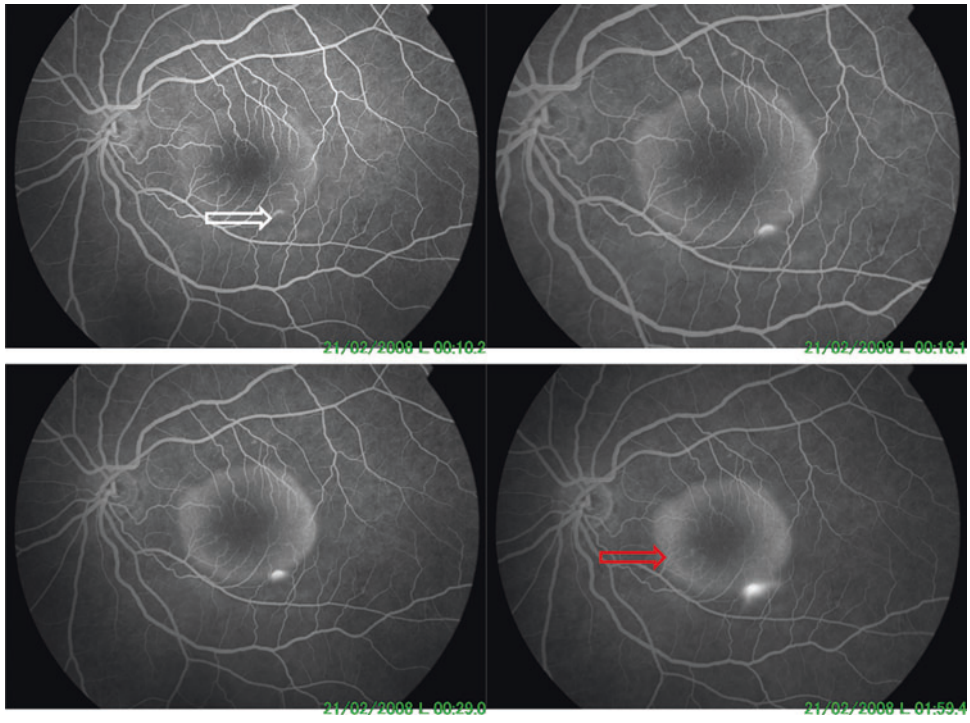
Common findings in CSC include a delay in choroidal filling, abnormal dilated choroidal vessels in the early stage, and choroidal hyperpermeability in the late phase (Fig. 3). The area of abnormality is often much larger than the area affected on FFA and is often observed on the contralateral eye. Patches of hyper-fluorescence in the later stages are caused by leakage into the deeper choroidal layers. Hypo-fluorescent areas on ICG are likely to represent areas of choroidal non-perfusion, a possible pathogenic mechanism for this disease (Fig. 3).

Fundus Autofluorescence Imaging (FAF)

Fundus autofluorescence (FAF) that employs the use of either fundus cameras or confocal systems has also been used to further characterize CSC. Autofluorescent properties such as lipofuscin can release light when stimulated by certain wavelengths. In acute CSC, hyper-autofluorescence develops in the areas of the subretinal fluid due to unphagocytosed photoreceptor outer segments; however this may sometimes be blocked by the macula pigment. A hyper-autofluorescent border around the detachment, which is more marked inferiorly, may disappear on resolution of the CSC (Fig. 6). Other areas of focal hyper-autofluorescence correspond to punctate

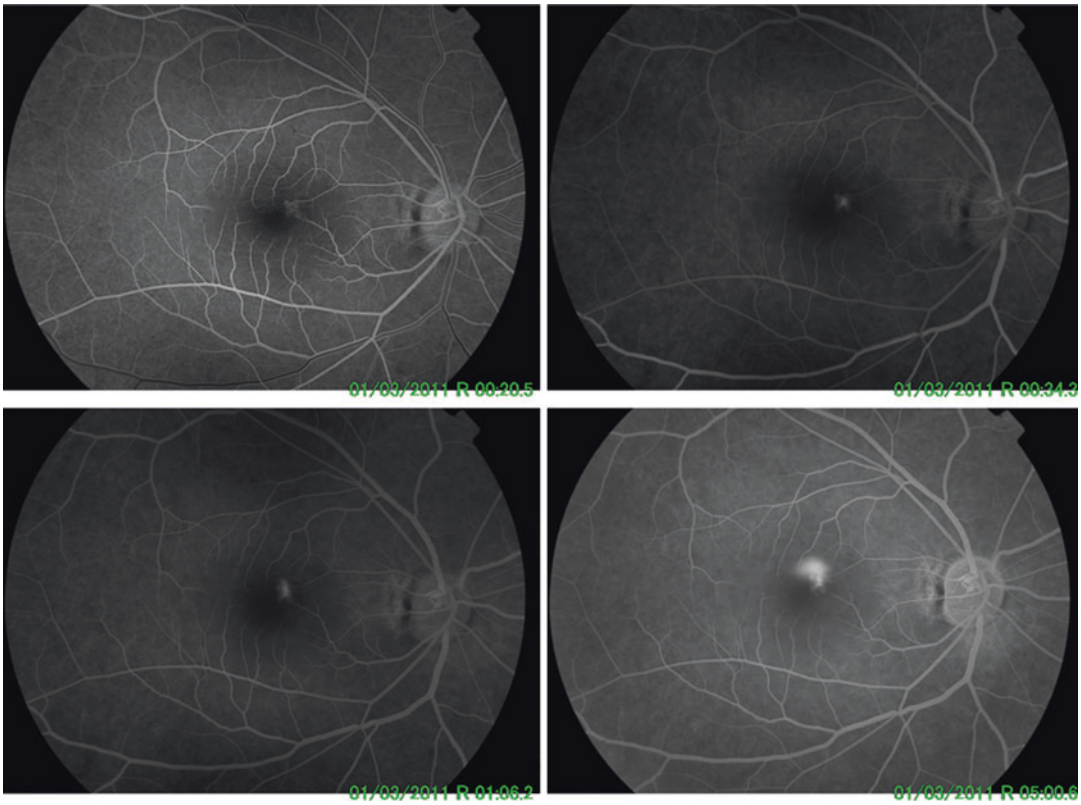


Central Serous Chorioretinopathy/Choroidopathy, Fig. 11 Fundus photo and FAF showing the confluent hypo-autofluorescence pattern in areas of RPE atrophy



Central Serous Chorioretinopathy/Choroidopathy, Fig. 12 FFA showing an "ink blot" pattern of leakage of the CSC. Early phases show the filling of the PED (*white arrow*), and then in the later stages, there is leakage into the subretinal space allowing the neurosensory detachment to be hyperfluorescent (*red arrow*)

precipitates and yellow-white deposits seen clinically and on OCT. In chronic CSC or DRPE, changes on FAF are due to RPE damage as well as areas of active serous detachment. Patterns previously described are granular (Figs. 8b and 9) or confluent hypo- or hyper-autofluorescence (Fig. 11). Descending tracts from the macula and optic nerve caused by the movement of subretinal fluid due to gravity can also be imaged on FAF (Fig. 8b). Correlation of FAF and OCT studies



Central Serous Chorioretinopathy/Choroidopathy, Fig. 13 FFA showing a "smokestack" pattern leakage of the CSC where dye from the sub-RPE space leaks through a breach in the RPE seen in the early phase, then flows upward into the subretinal exudate in an umbrellalike pattern in later phases

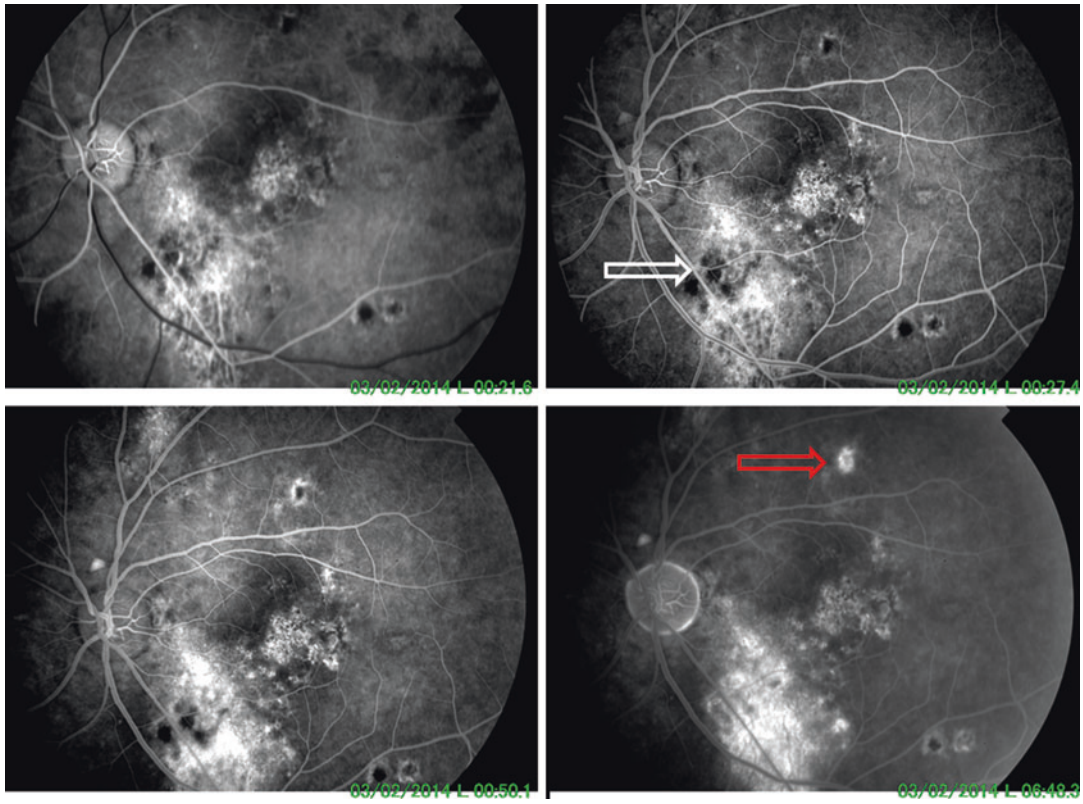
show that the areas of hypo-autofluorescence correspond to the areas of RPE atrophy and can be correlated with visual acuity if the central macula is affected. A granular FAF pattern was suggestive of incomplete RPE loss. Hyper-autofluorescence was not found to correlate significantly with visual acuity (Ryan 2012).

Multifocal Electroretinography (mfERG) and Microperimetry

Functional testing in CSC patients has shown reduction in amplitudes on mfERG with outer retinal dysfunction more marked in the central retina and inner retinal dysfunction more widespread extending into the periphery, and this can be correlated with visual acuity (Agarwal 2012). Implicit times show correlation with OCT findings in the paracentral rings. After subretinal fluid resolution, mfERG amplitudes improve, but do not return to normal. Macula sensitivity as measured by microperimetry correlates with findings on the OCT. Retinal sensitivity decreases with increased disruption of the EZ zone. Microperimetry has also shown a correlation to both mfERG implicit times and visual acuity. Similar to mfERG in CSC patients, retinal sensitivity does not return to normal despite the complete resolution of subretinal fluid and 20/20 visual acuity (Ryan 2012).

Adaptive Optics (AO)

AO allows the imaging of individual photoreceptors and was used in patient with previously spontaneously resolved CSC. There was a significantly lesser cone density in these patients compared to controls, despite most patients having 20/20 vision or better. The cone densities correlated with the visual acuity and with an intact EZ line on OCT (Ryan 2012).



Central Serous Chorioretinopathy/Choroidopathy, Fig. 14 FFA of a chronic recurrent multifocal CSC associated with steroid use, showing a window defect in areas of RPE atrophy (*white arrow*) and a superior area of leakage (*red arrow*)

Differential Diagnosis

In the majority of the time, the diagnosis of CSC can be made through a detailed history, slit-lamp microscopy, and OCT. However other diseases such as a congenital optic disc pit, choroidal tumors (e.g., hemangioma, osteoma, malignant tumors), uveal effusion syndrome, and other inflammatory diseases of the choroid (e.g., Vogt-Koyanagi-Harada disease, sarcoidosis, posterior scleritis) can be associated with serous detachments. Systemic diseases like malignant hypertension, toxemia of pregnancy, and disseminated intravascular coagulopathy can also be associated with a neurosensory detachment. Autoimmune diseases like systemic lupus erythematosus and polyarteritis nodosa can cause serous detachment from the disease itself or the subsequent treatment with corticosteroids. Age-related macular degeneration and polypoidal choroidal vasculopathy can commonly mimic CSC and must be considered in all elderly patients above 50 years old. Ocular contusion from trauma as well as traction from an incomplete posterior vitreous detachment can also resemble a serous detachment. In patients with chronic inferior retinal detachments, the diagnosis of retinoschisis, uveal effusion, or rhegmatogenous retinal detachment should be considered. Occasionally, after scleral buckling procedures, there may be a couple of residual pockets of exudative retinal detachment which may appear similar to CSC, (Agarwal 2012; Ryan 2012).

Therapy

Acute CSC is a self-limiting disease that usually requires no treatment. Risk factors like psychosocial

stressors should be minimized. Patients should be screened for CSC inciting drugs like corticosteroids, catecholamines, and 5-phosphodiesterase inhibitors and discontinue any unnecessary medication. The use of traditional herbal remedies and supplements, which may potentially contain corticosteroids, should also be discontinued. In cases of systemic autoimmune disease requiring immunosuppression, steroid-sparing agents should be considered as an alternative, and a slow tapering off of the steroids should be comanaged with a physician (Agarwal 2012; Ryan 2012; Liew et al. 2013; Nicholson et al. 2013).

In cases with no resolution in 3–4 months, chronic cases, or recurrent cases with progressive vision loss or in patients with high visual demands requiring rapid recovery, treatment can be considered. The main aims of treatment are to improve both structural and functional outcomes. The improvement of symptoms, visual acuity, and the size of the neurosensory detachment on OCT are all parameters used in clinical practice to assess recovery and treatment effect. The visual potential and the degree of swelling should be considered when planning treatment. For example, if there is extensive atrophy in the macula and scarring, there may be limited benefit from treatment; on the other hand, treating to remove chronic subretinal fluid may prevent further deterioration. Throughout the course of treatment, there is a risk of the development of secondary CNV, and this should be diagnosed and treated early to prevent further vision loss. Signs of retinal or subretinal hemorrhages and hard exudates adjacent to the neurosensory detachment or PED may suggest CNV.

Laser Photocoagulation

The best current evidence-based treatment of CSC is laser photocoagulation of extrafoveal areas of leakage or photodynamic therapy (PDT) for areas nearer the fovea. Laser has been thought to hasten the resolution of CSC, but does not affect the final visual acuity in most patients. FFA is required to identify focal areas of leakage, and laser burns are applied accordingly. In general, focal laser is only recommended in cases with an extrafoveal (>375 μm) focal area of leakage on FFA angiography. Diffuse leakage and focal leakage on FFA nearer the fovea should not be treated, due to the risk of scarring and atrophy. The aim of the laser is to stimulate the RPE to absorb to subretinal fluid and to stop further leakage. The exact mechanism of action is unclear. Randomized controls studying focal laser treatment to extramacular leakage sites shows a faster resolution of subretinal fluid but no improvements in visual acuity when compared to controls. There was also no improvement in recurrence rates after focal treatment. Secondary CNV after focal laser treatment was reported as a potential complication, and patients receiving focal laser should receive long-term follow-up.

Photodynamic Therapy

Photodynamic therapy that is directed toward the hyper-permeable choroid vessels has been shown to be safe and effective in the treatment of CSC. This treatment can promote the resolution in acute CSC and also prevent recurrences. The proposed mechanism of action is choroidal remodeling and thinning of the treated choroid. In trials using PDT to treat neovascular age-related macular degeneration, PDT was used to cause vaso-occlusion of the choroidal neovascularization. In contrast for CSC, treatment with PDT is required only for remodeling of the choroidal vasculature. Hence, modifications to the PDT dosage and laser energy aim to adequately treat CSC while reducing potential adverse effects. In a previous randomized controlled trial, half-dose PDT in patients with acute CSC has been shown to reduce the risk of persistent subretinal fluid at 1 year compared to controls. All patients of the treatment group had a visual acuity that was stable or improved in compared to only 78.9% of the control group. Other studies have shown that in some patients, multiple sessions of PDT may be required to achieve complete fluid resolution; however this should be balanced against the risk of chorioretinal atrophy. In one study, the risk of chorioretinal atrophy was found to be greater in the PDT-treated eyes than the eyes treated with focal laser, leading to vision loss in some patients. In addition, secondary CNV, choroidal ischemia, and RPE rips were reported as other potential complications. Hence, reduced fluence treatment that can

be achieved by reducing the laser treatment time, lowering the laser power or increasing the interval between infusion and laser, and reducing the verteporfin dose may be a safer alternative. It is debatable whether PDT should be performed under FFA or ICG guidance. A spot size large enough to cover the area should be applied avoiding areas of significant RPE atrophy (Ryan 2012; Nicholson et al. 2013). In some studies, a significant reduction in the choroidal thickness as seen on enhanced depth OCT is seen in the eyes treated with PDT, but a similar change is not observed in the eyes treated with focal laser.

Anti-VEGF Therapy

VEGF levels were not found to be elevated in the aqueous or plasma in patients with CSC; however small reports of improvements in both anatomical and functional parameters in CSC have been reported after the treatment with anti-VEGF agents. However, anti-VEGF agents did not seem to have better outcomes when compared to PDT. Hence when the two treatments are compared, the efficacy and safety of intravitreal injections are questionable.

Other Therapies

Other forms of laser therapy like diode micropulse laser and transpupillary thermotherapy have been trialed in other smaller studies with a limited follow-up duration. Overall these therapies show a benefit in the resolution rate of CSC but variable improvements in visual acuity and function. However, there is insufficient evidence to support the safety and efficacy of these treatments.

Elevated serum cortisol levels are related to the underlying pathogenesis of CSC. Anti-glucocorticoids, which inhibit the cortisol pathway such as ketoconazole, mifepristone, finasteride, rifampicin, and anti-adrenergics, have been trialed in small studies with variable results. Further studies are needed to confirm a significant benefit. Beta-blockers that cause an adrenergic blockade have been investigated for CSC but have not shown to be effective.

Carbonic anhydrase inhibitors (CAIs) have been used to treat CSC, on the basis that it can increase subretinal fluid reabsorption and retinal adhesion at the level of the RPE. Only one study on CAIs has shown that there was a faster resolution rate of acute CSC but no difference between visual acuity and recurrence rates between treatment group and controls. Similarly, the treatment of *H. pylori* with systemic antibiotics in *H. pylori*-positive CSC patients showed faster resolution of disease but no visual acuity improvement when compared to controls (Ryan 2012). Hypercoagulability has been proposed as another potential mechanism of CSC, and in one study, aspirin was shown to improve the rate of recovery, reduce rate of recurrence, and result in slightly better visual acuity when compared to controls (Ryan 2012; Nicholson et al. 2013).

One small pilot study with no controls has reported an improvement in both central macular thickness and visual acuity in cases of chronic CSC after treatment with eplerenone, a mineralocorticoid receptor antagonist. A few larger randomized control trials are underway to determine the efficacy and safety of this promising medical treatment for chronic CSC (Bousquet et al. 2013).

Prognosis

The natural history of this disease is that 90% of cases will show spontaneous recovery within a few months without significant vision loss. As mentioned before despite visual acuity recovery, subtle changes can still be seen clinically, on FAF, OCT, and mfERG. However in about 5% of CSC patients, visual acuity will not improve to 20/30 or better. Fifty percent of patients recur and this is more common in the first year. Especially in recurrent and chronic forms of CSC, where there is widespread RPE atrophy and scarring, irreversible vision loss with reduction in contrast sensitivity and color vision can occur. Poor prognostic factors for visual acuity include a poor presenting visual acuity and a prolonged duration of the neurosensory detachment. In a small group of patients (up to 6%), a secondary CNV can develop and cause visual loss. Spontaneous resolution of a small PED is more common than in larger lesions; however the visual acuity usually remains preserved despite a large PED. Despite complete resolution of a serous detachment, residual

pigmentary changes and mottling can still be observed. High-resolution imaging shows subclinical structural changes occur despite regaining 20/20 vision; hence CSC should not be considered a benign disease (Agarwal 2012; Ryan 2012).

Epidemiology

The incidence rates of CSC in the largest population-based study in Minnesota, USA, were estimated as 9.9 cases per 100,000 in men and 1.7 cases per 100,000 in women. CSC is thought to have a higher incidence in Asian populations followed by Caucasian populations and affects African-Americans the least (Ryan 2012; Liew et al. 2013). In one study with Chinese Singaporeans, the rates of multifocal and bilateral involvement of CSC were higher than in a similar white population. Another study reported that despite lower rates in African-Americans, these patients have worse visual acuity throughout the course of disease suggesting a greater severity of the disease (Liew et al. 2013).

CSC is more common in males than in females with previous ratio reported as 6:1. The age of onset ranges between 30 and 50 years of age. Older CSC patients tended to have a higher rate of chronic CSC with diffuse RPE loss and sometimes the development of secondary choroidal neovascularization (CNV) (Ryan 2012).

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Central Stromal Crystalline Corneal Dystrophy

▶ Schnyder Crystalline Dystrophy Syndrome

Cerebelloretinal Hemangioblastomatosis

▶ Hemangioblastomas, with Retinal Angiomatosis (von Hippel Lindau Disease)
▶ Retinae (Retinal Angiomatosis, von Hippel Syndrome/Disease)
▶ VHL Syndrome

Cerebral Achromatopsia

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History

Cerebral achromatopsia was first reported in the late 1800s and was initially described as the result

of damage to the "color center" of the brain (Danchaivijitr and Kennard 2008).

Definition

Complete achromatopsia is the inability to identify color; everything an individual perceives is monochrome: black, white, and shades of gray. Cerebral achromatopsia is unique because the loss of color vision is due to damage to the cerebral cortex. It may result in complete loss of color vision, or in some cases, patients miss one primary color (Lawton and Wang 2014). Bilateral lesions cause complete cerebral achromatopsia; unilateral lesions cause hemiachromatopsia, which is often unnoticed by patients (Boyd and Matsuba 2011). However, it is perceived when it is tested directly (Paulson et al. 1994). Patients with cerebral achromatopsia generally describe objects as "washed out" or "faded," and they see many shades of gray (Lawton and Wang 2014).

Etiology

Bilateral damage to a relatively small region of the cortex – the inferior surface of the temporal–occipital regions, in particular the lingual and posterior fusiform gyri (Bovier 2006). The most common cause of cerebral achromatopsia is an embolic stroke in the territory of the posterior cerebellar artery. It can also be caused by physical trauma and abnormal tissue growth (tumor). Other conditions such as carbon monoxide poisoning and cerebral metastases have also been reported to cause cerebral achromatopsia (Danchaivijitr and Kennard 2008).

Classification

The two most common classifications for cerebral achromatopsia are complete and hemifield. Complete loss of color vision results from a bilateral lesion, and hemifield is characterized by homonymous hemiachromatopsia, which is contralateral to the single cerebral cortex that is lesioned. In uncommon cases superior or inferior homonymous quadrantachromatopsia has been recorded. In still rarer cases, transient cerebral achromatopsia has been reported due to temporary ischemia (Danchaivijitr and Kennard 2008).

Cross-References

▶ Blue Cone Monochromatism
▶ Dyschromatopsia

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Cerebral Akinetopsia

▶ Akinetopsia

Cerebral Venous Sinus Thrombosis (CVST)

▶ Dural Sinus Thrombosis

Cerebrohepatorenal (Zellweger) Syndrome

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Synonyms

Cerebrohepatorenal syndrome; Zellweger syndrome

Definition

The peroxisomal biogenesis disorders are autosomal recessive disorders that include cerebrohepatorenal syndrome (Zellweger syndrome), adrenoleukodystrophy, infantile Refsum's disease, and Alagille syndrome. These disorders are characterized by abnormal oxidation and toxic accumulation of very long-chain fatty acids.

Cerebrohepatorenal syndrome is the most severe and most common peroxisomal disorder of early infancy affecting 1 in 50,000 live births. It is characterized by craniofacial dysmorphism and profound neurologic abnormalities with infants rarely surviving beyond the first year of life. Systemic findings include muscular hypotonia, seizures, poor feeding, sensorineural hearing loss, deficient cerebral myelination, renal cysts, and hepatomegaly.

Ocular findings are diverse and include hypertelorism, shallow supraorbital ridges, epicanthal folds, microphthalmia, nystagmus, corneal clouding, cataract, glaucoma, and optic disc atrophy. Brushfield spots, focal areas of stromal hyperplasia on the iris periphery, have also been described in these patients. Retinitis pigmentosa-like retinopathy has also been reported in patients with Zellweger syndrome, characterized by severe, infantile-onset retinal dystrophy with retinal hypopigmentation and vascular attenuation. The electroretinogram is either profoundly abnormal or completely absent, and visual evoked potential (VEP) responses are prolonged. Nystagmus and strabismus are common, secondary to poor vision.

Increase of plasmatic very long-chain fatty acids serves as a biochemical marker for this syndrome. Definitive diagnosis is made via DNA testing.

Currently, no effective treatment is available for Zellweger syndrome. Docosahexaenoic acid supplementation has been suggested as a possible therapy though its benefit is still controversial.

Cross-References

- ▶ Cataract, Causes and Treatment
- ▶ Developmental Glaucoma
- ▶ Microphthalmia
- ▶ Optic Atrophy

Cerebrohepatorenal Syndrome

- ▶ Cerebrohepatorenal (Zellweger) Syndrome

Cerebrovascular Accident (CVA)

- ▶ Monocular Transient Visual Loss, Stroke After

Ceroid Lipofuscinosis

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Synonyms

Batten disease; Neuronal ceroid lipofuscinosis

Definition

The neuronal ceroid lipofuscinoses (NCLs) are a group of autosomal recessive disorders caused by lipofuscin accumulation within the lysosomes of cells leading to cellular dysfunction and cell death. The approximated incidence is 1 per 12,500 live births. The disorders are associated with variable, yet progressive, symptoms including progressive degeneration of the nervous system, cognitive and motor decline, seizures, visual loss, and early death.

Clinically, the childhood-onset disorders have been classified into infantile, late-infantile, and juvenile forms based primarily on the age of symptom onset, rate of disease progression, and pattern of symptoms. The infant and juvenile types are associated with ocular findings in general and pigmentary retinopathies specifically, while the adult forms of NCL are absent ocular manifestation. More recently, following identification of several genetic mutations resulting in this condition, newer classifications have been suggested based on the affected gene.

One of the earliest signs of NCL may be vision loss associated with outer retinal degeneration. Typical ocular findings in infantile NCL include optic disc atrophy, hypopigmentary changes of the retinal pigment epithelium (RPE) in the macular area with mottling of the fundus periphery. The late-infantile and juvenile onset subtypes typically show a macular granularity or a bull's eye maculopathy, with variable degrees of peripheral RPE change, optic disc atrophy, and attenuation of the retinal blood vessels. Fluorescein angiography of juvenile patients demonstrates diffuse RPE atrophy with stippled hyperfluorescence. All NCLs show a profoundly abnormal or absent electroretinogram.

The diagnosis of NCLs is made on clinical grounds and by demonstrating characteristic curvilinear, fingerprint, or granular inclusions on electron microscopy of a peripheral blood smear or conjunctival or other biopsy tissue.

No specific systemic or ocular treatments are currently available for this group of disorders.

Cross-References

- ▶ Angiography, Fluorescein
- ▶ Electroretinogram
- ▶ Optic Atrophy
- ▶ Retinal Pigment Epithelium

Chalazion

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Synonyms

Meibomian cyst; Meibomian gland lipogranuloma; Posterior blepharitis; Zeis gland cyst

Definition

A chalazion is a noninfectious, lipogranulomatous reaction within the eyelid sebaceous glands (Cohen et al. 2001; Canninga-Van Dijk 2006; Friedman and Kaiser 2007; Lambreghts and Melore 2008; Shields and Shields 2008).

Etiology

A chalazion results from a noninfectious obstruction of the sebaceous gland ducts. Sebum accumulates and leaks into the surrounding tissue resulting in acute inflammation that leads to a chronic lipogranulomatous reaction. Chalazion can also result from an internal hordeolum (Lambreghts and Melore 2008). It is associated with poor lid hygiene, chronic blepharitis, and acne rosacea (Friedman and Kaiser 2007).

Histopathological evaluation demonstrates fatty cells within a granulomatous reaction (Canninga-Van Dijk 2006). A connective tissue pseudocapsule is often seen around the lesion. Causative organisms are usually not found, as the reaction is by definition a sterile inflammation, but secondary infections may occur.

Clinical Presentation

Chalazia initially present with tender, erythematous swelling of the eyelid and in late stages develop into a firm, painless nodule palpable to the patient and examiner (Lambreghts and Melore 2008). Patients may present at any stage; slit-lamp examination demonstrates meibomian gland disease and a papillary reaction with hyperemia of the palpebral and tarsal conjunctiva. Manual pressure on the eyelid margins may result in expression of thick, toothpaste-like secretions from meibomian glands. Patients often describe a history of previous chalazia (Cohen et al. 2001).

Diagnosis

Diagnosis of chalazion is based on a combination of history and clinical examination. Recurrent chalazia should raise suspicion for sebaceous cell carcinoma and require biopsy of the eyelid and conjunctiva (Cohen et al. 2001).

Differential Diagnosis

A stye, or external hordeolum, differs from a chalazion in its location in the anterior eyelid and an infectious etiology, often staphylococcal in origin (Friedman and Kaiser 2007). Patients with stye typically experience greater tenderness, erythema, and discharge compared to chalazion, although both find benefit from hot compresses (Cohen et al. 2001).

Sebaceous cell carcinoma often mimics chalazion, and recurrent chalazia in the same location should be biopsied to rule out this potentially lethal eyelid malignancy. Multiple conjunctival map biopsies will be required due to its pagetiod spread through the conjunctival epithelium, and such patients should be referred to an oculoplastic specialist (Shields and Shields 2008).

Prophylaxis

Conservative treatment with hot compresses, lid scrubs, and mild lid massage may be helpful to reduce recurrence in most patients. In those with frequent recurrences, low-dose oral tetracyclines may assist with both infection and inflammation.

Therapy

Initial therapy includes hot compresses, lid scrubs, and eyelid massage to dilate gland orifices and assist in secretion of solidified meibum (Cohen et al. 2001). Topical steroids reduce inflammation and a short course can be given with appropriate follow-up to prevent a steroid response; intralesional steroid injection, such as triamcinolone, can be effective but may cause hypopigmentation of overlying skin (Lambreghts and Melore 2008). At the slit-lamp, secretions and miniscule soft, distal obstructions can be expressed through meibomian gland orifices with pressure at the eyelid margin from a cotton-tipped applicator; once inflammation has resolved, incision and curettage may be utilized to remove remaining granulomatous material.

Prognosis

Chalazia generally resolve medically or surgically without detriment to vision. However, large, central, upper-eyelid chalazia overlying the cornea in children may induce ptosis and astigmatism and should be addressed to reduce risk of amblyopia (Friedman and Kaiser 2007). Recurrence in multiple locations is not uncommon and patients should be counseled on good eyelid hygiene practices (Friedman and Kaiser 2007). Sebaceous cell carcinoma is potentially lethal and recurrent chalazia should be biopsied to exclude its presence.

Epidemiology

Men and women are equally affected. Chalazia are more commonly found in adults than children.

Cross-References

- External Hordeolum (Stye)
- Hordeolum
- Sebaceous Glands of Eyelid, Tumors Arising in

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Chandler Syndrome

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Synonyms

Iridocorneal endothelial (ICE) syndrome

Definition

The most common variant of ICE syndrome, which includes essential/progressive iris atrophy and Cogan-Reese syndrome, Chandler syndrome is characterized by proliferation of endothelial cells with subsequent microcystic corneal edema and beaten bronze appearance to the corneal endothelium. Notably, corneal edema is present despite normal or slightly elevated intraocular pressure and may be present early in disease. Iris nodules, which form early in Cogan-Reese syndrome, may appear late in Chandler syndrome. High peripheral anterior synechiae and glaucoma are characteristic of this disease.

Cross-References

- Angle-Closure Glaucoma
- Anterior Segment
- Cornea
- Iridocorneo Endothelial Syndrome

Further Reading

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Charcot-Marie-Tooth Disease, Retinal Degeneration

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Synonyms

Hereditary motor-sensory neuropathy retinal degeneration

Definition

Charcot-Marie-Tooth (CMT) disease is the most common inherited peripheral neuropathy with an

incidence of 1 in 2,500 live births. CMT is a demyelinating disorder comprised seven different major types with types 1 and 2 being the most common involving over 30 different identified genes. Patients typically present during early adulthood with motor and sensory peripheral polyneuropathy leading to distal leg weakness, foot deformities such as pes cavus or hammer toes, and sensory deficits. Ambulation is usually maintained throughout life, and life expectancy is not affected. The management of CMT is primarily supportive as specific disease-modifying therapy is not yet available.

Ocular symptoms are not invariably present. The most common ophthalmic symptoms are bilateral subacute deterioration of visual acuity accompanied by a central or paracentral *scotoma* and color vision abnormalities usually affecting the red-green axis. Ocular manifestations such as pupillary reflex abnormalities, premature *presbyopia*, *retinitis pigmentosa*, *optic atrophy,* and nystagmus have all been previously described in CMT. Fundus examination, depending on the precise genotype and phenotype, may demonstrate optic atrophy, attenuation of peripapillary blood vessels, thinning of the retinal nerve fiber layer, and signs of pigmentary retinopathy. Pathological reports indicate a pattern of retinal ganglion cell loss similar to Leber's hereditary optic neuropathy with preferential involvement of the papillomacular bundle, while the outer retina is usually not involved.

Visual field testing may demonstrate a central or paracentral scotoma. Fluorescein angiography may show signs of central tapetoretinal degeneration with macular pigmentary changes. Visual-evoked potentials usually show markedly reduced amplitude and delayed patterns. Electroretinographic recordings are usually within normal limits.

Cross-References

- ▶ Atypical Retinitis Pigmentosa (RP)
- ▶ Junctional Scotoma
- ▶ Optic Atrophy
- ▶ Presbyopia

Charles Bonnet Syndrome: Overview

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Synonyms

Complex visual hallucination; Visual release hallucinations; Visual release phenomena; Vivid visual hallucinations

Definition

Charles Bonnet syndrome (CBS) is a common cause of complex visual hallucination occurring in patients with variable degrees of visual impairment and in the absence of alternative secondary causes (e.g., hallucinogenic drug use, delirium, mental illness). Its prevalence varies from 10% to 15% in visually impaired patients and is probably under recognized. It was named after the Swiss naturalist and philosopher Charles Bonnet (1720–1792) whose grandfather experienced these types of formed visual hallucinations (e.g., people, birds, and buildings).

Etiology

Although numerous theories have been suggested to explain CBS, its pathophysiology

remains poorly understood. It has been hypothesized however that reduced or absent visual stimulation causes an increased excitability of the sensory cells that continue to generate perceptual visions that had been already stored in the brain visual cortex (deafferentation theory). CBS release phenomenon is possibly analogous to "phantom limb" symptoms after an amputation in which a person might perceive pain and sensation of the amputated limb. CBS predominantly affects patients with moderate or severe visual impairment particularly with bilateral and central vision loss and can be precipitated by or associated with simultaneous illness infections or older age. Multiple etiologies have been associated with the visual loss in CBS including diabetes, optic nerve damage, macular degeneration, and glaucoma.

Clinical Presentation

Although there are no universally accepted diagnostic criteria for CBS, patients typically report formed, vivid, and frequently stereotyped visual hallucinations in the setting of prior visual impartment. Patients typically have some or total insight that the visual hallucinations are imaginary and unreal. An alternative diagnosis to CBS however should be considered first if any of the following is present: psychosis, dementia, intoxication, altered mental status, focal neurological signs, auditory hallucinations, or underlying metabolic derangements. CBS most commonly affects elderly people with visual impairment (most commonly age-related macular degeneration, glaucoma, and cataract).

The descriptions of the visual hallucinations vary from groups of people or animals, figures, or forms, and usually they have no personal meaning, underlying context, or symbolic interpretations. Each episode may last from few seconds to days. Many patients have chronic symptoms that may wax and wane or even improve after several months. Interestingly, some patients with progressive visual loss might even improve after the vision is totally lost.

Diagnostics

CBS is a diagnosis of exclusion. Gold and Rabins recommended the following diagnostic criteria of CBS: (1) formed, repetitive, complex, and stereotyped visual hallucinations, (2) the retained insight into the unreal nature of the visual hallucinations, (3) the absence of delusions, and (4) the absence of other modalities of hallucinations. Degree of visual impairment was not included within their diagnostic criteria, but most of studies report some relation between the severity of visual impairment and the risk of CBS.

Differential Diagnosis

1. Schizophrenia
2. Delirium tremens
3. Dementia
4. Complex partial seizures
5. Recreational drug abuse
6. Parkinson disease or other neurodegenerative disease (e.g., Lewy body) with visual hallucinations
7. Hypnagogic and hypnopompic hallucinations
8. Migraine aura
9. "Alice in Wonderland" syndrome

Prophylaxis

Not applicable

Therapy

Although there is no treatment with proven benefit for CBS, it is crucial to appropriately make the diagnosis and exclude treatable or alternative conditions. Most patients only wish to have reassurance that it is not an underlying psychiatric disorder. Treating comorbidities and lifestyle modifications may also be helpful (e.g., reducing social isolation and encouraging interpersonal contact).

Treatments with antipsychotics, antimigraine agents, and anticonvulsants may be helpful in

selected cases (e.g., risperidone, valproate, carbamazepine, clonazepam, gabapentin, olanzapine, and selective serotonin reuptake inhibitors).

Prognosis

The prognosis of CBS is variable and may remit spontaneously or with treatment. Treatment of the visual impairment if possible is recommended, and there have been cases where cataract extraction and recovery of vision lead to improvement in CBS.

Epidemiology

Patients with visual hallucinations due CBS often fail to report their symptoms to their physician or their family members because of the fear that they represent a psychiatric disease. The prevalence of CBS varies from 12% to 15% of visually impaired patients. The mean age is between 70 and 85 years.

Cross-References

Not applicable

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Chédiak-Higashi Syndrome

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C

Synonyms

Partial oculocutaneous albinism

Definition

Chédiak-Higashi syndrome (CHS) is an autosomal recessive disorder among the spectrum of partial oculocutaneous albinism, in which hypopigmentation of the skin and eyes is associated with immunodeficiency. Clinical findings include increased susceptibility to infection, especially bacterial, coagulation defects, and progressive peripheral neuropathy. Ultimately, a severe disease stage occurs in which massive lymphohistiocytic infiltration of organs termed "accelerated phase" results in death in the first decade of life. CHS is a rare disorder, with less than 500 reported cases in the past two decades, caused by a fundamental defect in granule genesis, leading to abnormally large granules in multiple tissues. Mutations in the CHS1/LYST gene, encoding a family of proteins thought to regulate lysosomal trafficking and degranulation, have been identified in CHS patients.

The pigmentary dilution involving the hair, skin, iris, and ocular fundus is the result of a pathologic aggregation of oversized melanosomes that fail to disperse to the target organs. Patients typically have silvery gray hair and blue irides. Ocular symptoms include photophobia and decreased visual acuity which may result from high refractive error, iris transillumination defects, retinal pigment epithelium (RPE) degeneration, and foveal hypoplasia. Rotary nystagmus and strabismus, often present at birth, may be related to abnormal decussation

of the optic nerve fibers from the temporal retina to the contralateral cerebral hemisphere and may also correlate with the degree of foveal hypoplasia.

Clinical diagnosis is supported by the presence of peroxidase-positive giant inclusions in white blood cells, by detection of pigment clumping in the light microscopy analysis of hair, and eventually by studies revealing abnormal platelet aggregation. A definitive diagnosis requires genetic testing for mutations in the CHS1/LYST gene on chromosome 1.

No specific ocular treatment is available. Refractive errors should be corrected, and some patients benefit from bifocal lenses. If visual acuity is severely impaired, these patients can be helped with telescopic and other low-vision devices. Strabismus surgery for esotropia or exotropia can be considered for better ocular alignment.

The most effective treatment for the hematological and immune defects of CHS is hematopoietic stem cell transplantation, although little evidence of efficacy in delaying or preventing neurological dysfunction exists.

Cross-References

- ▶ Fundus Oculi
- ▶ Optic Nerve (Cranial Nerve II)
- ▶ Retinal Pigment Epithelium

Cheek Elevation, in Eyelid Repair

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Synonyms

Midface lift; Preperiosteal midface lift; SOOF lift; Subperiosteal midface lift

Definition

Elevation of cheek and midface tissues with the goal of anterior lamellar recruitment (skin and muscle) for lower eyelid repair when anterior lamellar shortage is present.

Indication

Posttraumatic or post-cancer excision (including Mohs surgery) defects of the lower eyelid with resultant anterior lamellar shortage requiring skin recruitment to repair the defect can be addressed with midface/cheek lift surgery. Other options include local myocutaneous advancement flaps and full-thickness skin grafts. In addition to its utility in reconstructive surgery, cheek/midface lift surgery is sometimes performed as an aesthetic procedure to improve the youthfulness of the cheek and midface region.

Contraindication

Cheek/midface elevation adds to surgical operating time as well as surgical complexity. Adequate skin recruitment may not be achievable with cheek/midface elevation alone in cases of large defects.

Techniques and Principles

When utilized in eyelid repair surgery, the goal of cheek/midface lifting is to recruit anterior lamellar tissues (skin and muscle) for lower eyelid reconstruction. There are a variety of techniques utilized in cheek/midface lift surgery, which can be broadly categorized based on the plane of dissection and the incisional approach. The plane of dissection of the cheek/midface lift can be either subperiosteal or preperiosteal. A variety of incisional approaches to the midface exist including transconjunctival, subciliary, sublabial, and temporal approaches. Endoscopic guidance can also be used to improve visualization, particularly when using a temporal approach.

Preperiosteal cheek/midface lift begins with the desired incisional approach; a transconjunctival

approach is most common. A preperiosteal plane is then carried inferiorly until adequate freeing and superior mobilization of the cheek/midface is achieved to allow for eyelid reconstruction. Care is taken to spare the infraorbital neurovascular bundle and to avoid the branches of the facial nerve, which lie just above this preperiosteal plane. The midface tissues are then lifted and secured to the periosteum of the infraorbital rim with sutures.

The subperiosteal cheek/midface lift can often provide a more robust superior lift as compared to a preperiosteal cheek/midface lift. The subperiosteal cheek/midface lift begins with the desired incisional approach; a transconjunctival approach is most common. Dissection is carried down to the arcus marginalis of the inferior orbital rim, and an incision is then created through the periosteum to gain access to the subperiosteal space. Freeing of the entire midface is then performed in this plane. Care is taken to avoid injury to the infraorbital neurovascular bundle. A periosteotomy is created medially along the piriform aperture, inferiorly along the alveolar ridge, and laterally along the masseter muscle to allow complete midface mobility. The midface is then lifted superiorly and secured to the arcus marginalis of the infraorbital rim with sutures.

Regardless of the plane chosen or the incisional approach, the goal of cheek/midface lift surgery in eyelid repair remains the same, recruitment of anterior lamellar tissues superiorly to allow for eyelid reconstruction.

Outcome

Elevation of the cheek/midface tissues results in recruitment of vascularized anterior lamellar tissues, particularly the skin and muscle, for use in eyelid reconstruction.

Complications

Injury to sensory and/or motor nerves within the midface is possible. Secondary ectropion of the reconstructed lower eyelid can result if inadequate skin has been recruited or if downward tension on the lifted cheek/midface is present.

Cross-References

▶ Eyelid Reconstruction

References

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Cheek Rotation Skin Flap to the Lower Lid

▶ Mustarde Flap

Cheekbone

▶ Zygomatic Bone

Chelation Therapy, for Calcific Band Keratopathy

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Synonyms

Disodium ethylenediaminetetraacetic acid; EDTA chelation therapy

Definition

Procedure for the removal of calcium phosphate crystals from the superficial corneal layers

Indication

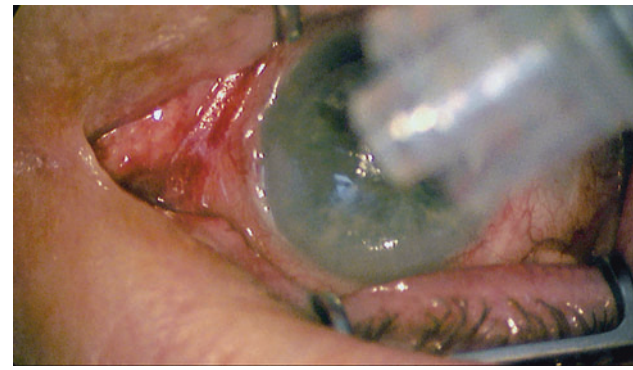
EDTA chelation therapy is the most commonly practiced method in the treatment of band keratopathy. Band keratopathy is characterized by deposition of calcium phosphate salts in the epithelial basement membrane, Bowman's membrane, and anterior stroma. It commonly occurs in the eyes with chronic diseases such as uveitis, keratitis, trauma, exposure to chemical toxins, intraocular silicone oil, sarcoidosis, glaucoma, and conditions associated with elevated serum calcium or phosphate.

Contraindication

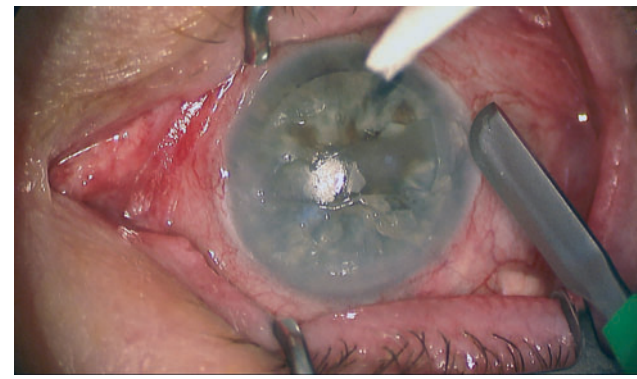
Limbal stem cell deficiency and neurotrophic keratopathy (relative contraindications)

Use and Dosage

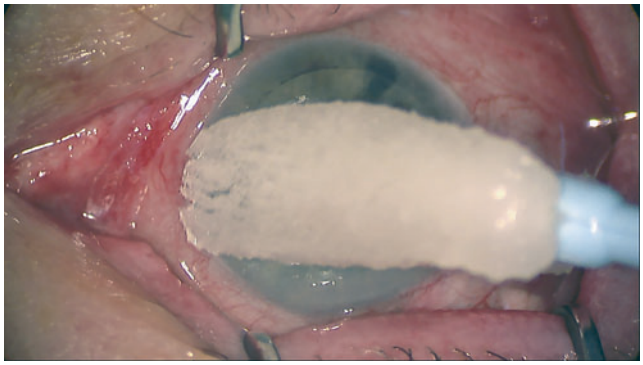
EDTA is prepared as a 3% solution by diluting disodium EDTA 15% (150 mg/ml) 1:4 with normal saline. A drop of topical anesthetic is instilled into the eye at the beginning of the procedure. Epithelial debridement is performed with a surgical blade. EDTA solution is then applied with a saturated cellulose sponge or cotton-tipped spatula. The solution forms chelation complexes with the calcium deposits and can then be removed with a surgical blade or a diamond burr. The procedure is repeated several times until the



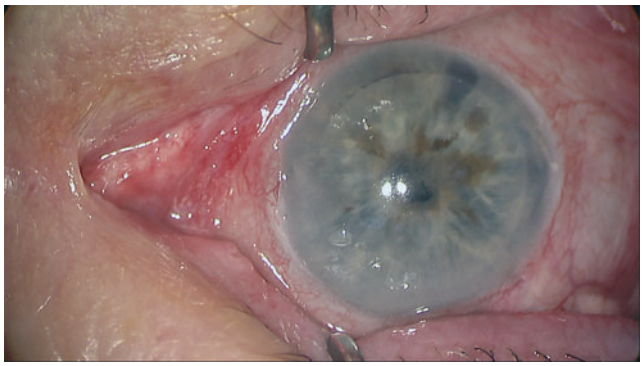
Chelation Therapy, for Calcific Band Keratopathy, Fig. 1 Instillation of topical anesthetic (Courtesy: Dr. Jeff Goshe and Dr. John Au)



Chelation Therapy, for Calcific Band Keratopathy, Fig. 2 Epithelial debridement (Courtesy: Dr. Jeff Goshe and Dr. John Au)



Chelation Therapy, for Calcific Band Keratopathy, Fig. 3 EDTA-soaked sponge is applied to the cornea and calcium deposits removed (Courtesy: Dr. Jeff Goshe and Dr. John Au)



Chelation Therapy, for Calcific Band Keratopathy, Fig. 4 Post procedure image (Courtesy: Dr. Jeff Goshe and Dr. John Au)

Bowman's membrane and anterior stroma are clear. At the end of the procedure, antibiotic ointment and a pressure patch are placed for several hours.

Adverse Reactions

No known adverse reactions

Interactions

No known interactions

Clinical Photographs

Figures 1, 2, 3, and 4

Further Reading

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Chemical Burns

▶ Chemical Injury (Burns)

Chemical Injury (Burns)

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Synonyms

Chemical burns

Definition

Exposure to acid or alkali whose severity of damage and ease of treatment are related to chemical toxicity, time of contact, depth of penetration, and area of involvement.

Acidic burns have a pH <7.4 and precipitate protein which acts as a potential barrier to deeper penetration and tissue destruction (Singh et al. 2013). Alkali burns have a pH >7.4 which causes saponification within cells of the ocular structure. An inflammatory response causes deeper tissue damage and limbal ischemia (Singh et al. 2013).

Etiology

Most acidic injuries are from household items, while alkali injuries in households and industry (Singh et al. 2013).

Clinical Presentation

The type of agent, toxicity of the agent, mechanism of injury, duration of contact, depth, and area of involvement should be collected. Use of protective eyewear should be carefully documented. Elevations in IOP should prompt immediate treatment (Wagoner 1997).

Clinical course is divided into immediate, acute, early, and late repair phase. The area of involvement is assessed by extent of fluorescein staining, depth of tissue injury, loss of stromal clarity, visual acuity, and observation of vascular ischemic and limbal necrosis. The immediate phase immediately follows chemical injury (Singh et al. 2013).

Acute phase of injury (day 1–7) is when epithelial migration occurs. The early repair phase (day 7–21 of injury) is marked by epithelialization. Limbal stem cell loss is evident by dysfunctional epithelialization. The late repair phase (day 21) is where conjunctivalization of the cornea occurs (Gupta et al. 2011).

Diagnosis

pH in the immediate phase of injury (Wagoner 1997).

Differential Diagnosis

Differential should include an open globe, local contact, thermal or radiant burns, or projectile tissue damage.

Prophylaxis

Use of protective eyewear and proper storage when handling corrosive or high-temperature substances.

Therapy

Obtain information from www.aapcc.org or by contacting poison control (Wagoner 1997). Immediate irrigation of the abnormal pH unless concern for an open globe exists. Copious irrigation with balanced solution using a Morgan Lens before clinical examination to return ocular structures to neutral pH. There is no difference between isotonic saline, lactated Ringer's, and saline with BSS; however, eyes irrigated with saline plus BSS have less pain. Once pH has been normalized, visual acuity, intraocular pressure, extent of perilimbal ischemia, and health of the corneal epithelium should be evaluated and treated (Wagoner 1997).

Treatment is based on grading with Roper-Hall or Dua classification (Gupta et al. 2011). Grade

I injuries are treated with a topical antibiotic with prednisolone acetate (QID). Grade II injuries are treated with antibiotics and more frequent use of prednisolone acetate. Oral supplementation with doxycycline 50 mg BID is also recommended. Placing punctual plugs might be considered and epithelial debridement might be required. Grade III is often treated with amniotic membrane transplantation within the first week of injury. More severe injuries classified as grade IV are treated with surgical intervention aimed at restoring limbal vascularity (Clare et al. 2012). The importance of serum drops at reducing inflammation can be tried. Injuries should be followed daily initially in the immediate and acute stage of healing with subsequent visits tapered to every few days until normal reepithelialization has occurred (Singh et al. 2013).

Prognosis

Clinical examination and visual prognosis is evaluated using the same Roper-Hall grade or Dua classification. While the Roper-Hall grading system is commonly studied and used to develop a standardized form of treatment, the Dua classification system is better aimed at determining visual prognosis.

Visual prognosis for RH grades I and II is good; however, visual prognosis for higher grades should remain guarded (Singh et al. 2013). The Dua classification is graded on a scale from I to VI involving clock hours of limbal involvement and percent of conjunctiva damaged with visual prognosis ranging from good to poor (Dua et al. 2001).

Roper-Hall (RH) grade of ocular surface burns is graded on a scale from I to IV. RH grade I injuries are described as eyes with corneal epithelial damage and no limbal ischemia. RH grade II includes eyes with corneal haze (with visible iris details) and $<1/3$ limbal ischemia. RH grade III includes total epithelial loss and stromal haze with iris details obscured with 1/3–1/2 limbal ischemia. RH grade IV involves an opaque cornea with iris and pupil obscured and $>1/2$ limbal ischemia. Generally, visual prognosis for grades I and II is good; however, visual prognosis for higher grades should remain guarded (Singh et al. 2013).

The Dua classification is graded on a scale from I to VI involving clock hours of limbal involvement and percent of conjunctiva damaged. Prognosis from classification I to VI is very good to very poor. Classification I involves no limbal or conjunctival involvement, with a visual prognosis that is "very good." Classifications II and III involve less than 3 clock hours of limbal involvement and $<30\%$ of conjunctiva or between 3 and 6 clock hours of the limbus with 30–50% of conjunctiva with a "good" visual prognosis. Classification IV involves a good to guarded prognosis in eyes presenting with between 6 and 9 clock hours of limbal involvement and 50–75% of the conjunctiva. Classification V involves between 9 and 12 clock hours of limbal involvement and 75–100% of the conjunctiva with a guarded to poor prognosis. Finally, classification VI has a very poor prognosis involving total limbus and total conjunctiva (Dua et al. 2001).

While the Roper-Hall grading system is commonly studied and used to develop a standardized form of treatment, the Dua classification system is better aimed at determining visual prognosis.

Epidemiology

Chemical injury represents 11–21% of total ocular traumas, mostly in young men between the ages of 20 and 40 years. Sixty-one percent of all chemical burns are industrial accidents in the workplace and 37% have been reported to occur in the home and in association with criminal assaults. Alkali injuries appear to occur more frequently than acidic (Clare et al. 2012).

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Chemical-Induced Optic Neuropathy

► Toxic/Nutritional and Hereditary Optic Neuropathy
► Toxic Optic Neuropathy

Chemosis

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Synonyms

Conjunctival edema

Definition

Chemosis is the swelling of the conjunctiva as a result of abnormal leaky conjunctival capillaries. It is typically a nonspecific indication of conjunctival irritation.

Etiology

In chemosis, the integrity of conjunctival capillaries is compromised, leading to increased permeability and leakage of serous fluid. Causes include conjunctival irritation, infection, inflammation, trauma, and severe intraorbital inflammation. The acute onset of chemosis is most commonly due to a hypersensitivity reaction, whereby an allergen irritates the conjunctiva and may lead to profuse rubbing of the eye. Chronic chemosis may indicate orbital outflow obstruction.

Causes include:

- Acute allergic conjunctivitis
- Conjunctivitis (viral or bacterial)
- Thyroid eye disease
- Orbital cellulitis
- Ocular trauma
- Carotid-cavernous fistula
- Cavernous sinus thrombosis
- Superior vena cava obstruction
- Post-ocular surgery
- Acute glaucoma
- Angioedema

Occurrence

Patients with chemosis frequently present with itchy or irritated eyes, particularly if caused by allergies. Other symptoms include tearing, blurry vision, and diplopia. The presentation may be asymptomatic in some cases. Chemosis appears as a localized or diffuse swelling of the conjunctiva. Depending on the severity, there can be incomplete eyelid closure. Conjunctival injection can also be present. Chemosis may cause corneal abnormalities, including exposure keratitis, superficial punctate keratitis, and Dellen formation.

Classification

In thyroid eye disease, the Vision, Inflammation, Strabismus, Appearance (VISA) inflammatory score incorporates a grading scale for chemosis:

0 – No conjunctival swelling present.
1 – Conjunctiva lies behind the gray line of the eyelid.
2 – Conjunctiva extends anterior to the gray line of the eyelid.

Cross-References

- ▶ Allergic Conjunctivitis
- ▶ Carotid Cavernous Fistula
- ▶ Cavernous Sinus Syndrome
- ▶ Conjunctiva
- ▶ Conjunctivitis
- ▶ Dellen
- ▶ Exposure Keratitis/Keratopathy
- ▶ Orbital Cellulitis
- ▶ Primary Angle Closure and Angle Closure Glaucoma
- ▶ Thyroid Eye Disease

Chiasmal Disorders

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Synonyms

Lesions of the optic chiasm; Parasellar lesions; Suprasellar mass lesions

Definition

A chiasmal disorder defined as any lesion that causes a disruption in the optic chiasm.

Etiology

The majority of optic chiasmal lesions in adults are caused by compressive suprasellar or parasellar lesions, such as:

1. Pituitary adenomas.
2. Craniopharyngiomas.
3. Meningiomas.
4. Internal carotid suprasellar aneurysm.
5. Dysgerminoma and hypothalamic/optic chiasmal glioma in younger patients.
6. Other infrequent causes of chiasmal disorders are demyelination (chiasmal neuritis), metabolic, toxic, traumatic, ischemic, infiltrative, inflammatory, or infectious.

The anatomical location of the optic chiasm (superior in relation to the sellae and inferior to the third ventricle) often determines the affected visual fibers and the visual defects. For example, a prefixed chiasm over the tuberculum occurs in 9%, the central body of the chiasm is directly above the pituitary in 80% (leading to the typical bitemporal hemianopsia), and is postfixed chiasm over the dorsum sellae 11%.

Clinical Presentation

The most common presenting symptom of chiasmal compressive lesions is a gradual, painless, progressive vision loss. Other less common symptoms are headache, diplopia from lateral extension of the lesion to the cavernous sinus, and concomitant ocular motor cranial neuropathies; endocrine dysfunction (from hypothalamic or pituitary lesions) may precede the visual symptoms (e.g., amenorrhea/galactorrhea, acromegaly, thyroid abnormalities, decreased libido, etc.).

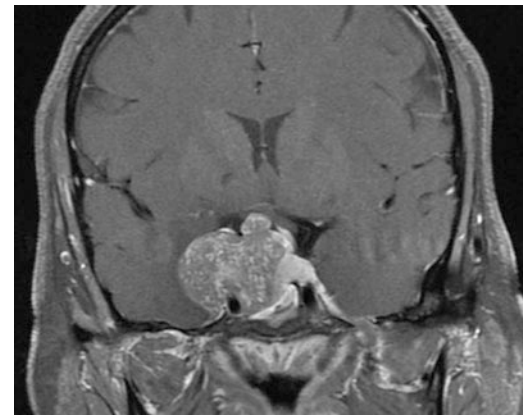
The most common visual field defect is bitemporal hemianopsia (complete, incomplete, symmetrical or asymmetrical) which accounts for 67% of the visual field defects due to compression of the crossing fibers of the chiasm and nasal fiber susceptibility at this location. Central scotoma (from concomitant unilateral or bilateral optic neuropathy), junctional visual field defect

(e.g., junctional scotoma and junctional scotoma of Traquair), or homonymous hemianopsia (optic tract) may occur but with less frequency.

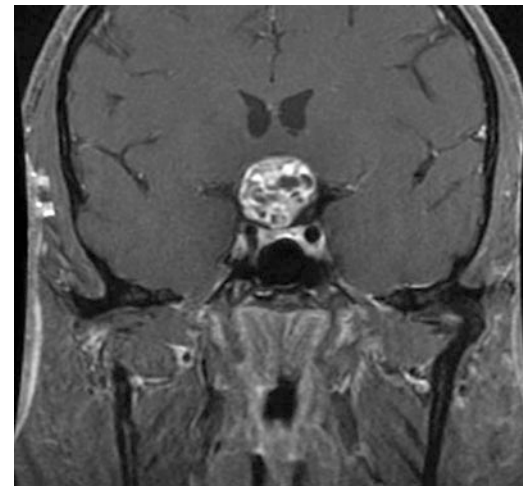
Although typically compressive chiasmal lesions produce subacute or chronic visual loss, an acute onset of bitemporal hemianopsia from chiasmal lesions may implicate a life-threatening emergency from a pituitary apoplexy or suprasellar aneurysm. Less commonly, demyelination or trauma can occur acutely. Pituitary apoplexy and suprasellar aneurysm are medical and neurosurgical emergencies that require prompt diagnosis and treatment. Apoplexy is typically characterized by an acute onset of severe headache, visual symptoms (impairment visual acuity and visual field), double vision (from cavernous sinus involvement), altered mental status, and hormonal dysfunction which is often associated with a life-threatening cortisol deficiency. Patients with chiasmal syndromes may have a relative afferent pupillary defect if a concomitant optic neuropathy or optic tract involvement is present. Slit lamp examination in patients with optic chiasmal glioma might show Lisch nodules in patients with neurofibromatosis 1. Motility exam might show ophthalmoplegia due to concomitant cavernous sinus involvement. Ophthalmoscopy may be normal or show optic atrophy depending on the etiology and duration of symptoms.

Diagnostics

Magnetic resonance imaging (MRI) of the brain with and without gadolinium (pituitary gland protocol) is the study of choice for the diagnosis of chiasmal disorders and can assist to distinguish between different lesions. The typical MRI features of a pituitary adenoma are hypointense to the brain on T1 and hyperintense on T2 with variable enhancement after gadolinium contrast (see Fig. 1). Craniopharyngioma is typically a cystic and solid heterogeneous mass in the suprasellar space that is isointense to lightly hypointense to the brain on T1 and shows variable/mixed on T2 and vivid enhancement on T1 post-gadolinium (see Fig. 2). Meningioma is typically isointense to the brain on T1 and T2 with vigorous, homogenous contrast enhancement with a dural tail.



Chiasmal Disorders, Fig. 1 Coronal MRI showing suprasellar pituitary mass hypointense to the brain on T1 and hyperintense on T2



Chiasmal Disorders, Fig. 2 Coronal MRI showing craniopharyngioma lightly hypointense to the brain on T1 and shows variable/mixed on T2

Computed tomography (CT) scan might be an adjunctive study to MRI in suprasellar lesions, hyperostosis or calcification (e.g., meningioma or craniopharyngioma) or might be the initial study in acute lesions or emergent settings like hemorrhage (e.g., pituitary apoplexy or aneurysm). Computed tomography angiography (CTA), magnetic resonance angiogram (MRA), and/or catheter angiography could still be

considered in case of radiographic findings suggestive of an aneurysm (e.g., a round lesion adjacent to the internal carotid artery with a flow void). Endocrinologic evaluation might be necessary in patients with suprasellar lesions.

Differential Diagnosis

The differential diagnosis of chiasmal lesions as mentioned in the etiologies section.

There are several conditions that mimic bitemporal hemianopsia:

1. Bilateral enlarged blind spot from peripapillary atrophy, the idiopathic big blind spot syndrome, papilledema, or posterior myopic staphyloma
2. The tilted optic disk syndrome

Prophylaxis

Non-applicable

Therapy

The treatment of the chiasmal lesion depends on the nature of the lesion. For instance, prolactin-secreting pituitary adenomas (i.e., prolactinoma) might be best treated medically with dopamine agonists (e.g., bromocriptine, cabergoline); demyelinating optic chiasmal neuritis might benefit from systemic corticosteroids; the most compressive lesions (e.g., pituitary adenoma, craniopharyngioma, and meningioma) require surgical intervention, but the approach and adjuvant or other chemotherapies or radiotherapies might be required. Transsphenoidal surgery has emerged as the best initial surgical treatment for symptomatic nonsecreting pituitary adenoma, but the surgical approach depends on the lesion type and location.

Radiation therapy (fractionated or by Gamma Knife) is reserved as an adjunctive therapeutic option for patients with non-resectable pituitary lesions (e.g., extensive cavernous sinus involvement), subtotal resections with risk of recurrence, or in patients who refuse or cannot tolerate a neurosurgical procedure. Craniotomy is generally not needed for most pituitary adenomas but may be necessary for other suprasellar lesions (e.g., craniopharyngioma, meningioma).

Pituitary apoplexy is a life-threatening emergency that typically requires admission to the hospital and emergent hormonal (corticosteroid) replacement.

Prognosis

The prognosis of a chiasmal lesion depends on the type of the lesion, size, and extension to adjacent structures and the duration of symptoms. Visually symptomatic pituitary adenoma may show stabilization or improvement after surgery in up to 94% of patients. In one series, authors noted that 25% had complete vision recovery and 50% had useful but incomplete vision recovery. Prognosis is correlated with the type of the tumor, patient age, duration of symptoms, size of the tumor, and presence or absence of optic atrophy. Optical coherence tomography (OCT) has arisen as a possible adjunctive tool for providing an objective prediction of visual prognosis and recovery.

Epidemiology

Pituitary tumors (pituitary adenomas) are the most common cause of chiasmal disorders with a prevalence as high as 75.7 per 100,000, and 47% were prolactinomas and 34% were nonfunctioning pituitary adenomas. There is no sexual predilection. Affected adults range in age from 30 to 40 years, but these tumors may occur at any age. Meningioma is typically a disorder of older-aged females but can occur in any age and either gender. Dysgerminoma and optic pathway glioma tend to affect younger individuals and aneurysms tend to affect older patients.

Cross-References

- ▶ Aneurysms
- ▶ Craniopharyngiomas
- ▶ Optic Gliomas

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Childhood Glaucoma

▶ Pediatric Glaucoma

Chlamydia

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Synonyms

Chronic follicular conjunctivitis; Inclusion conjunctivitis; Trachoma

Definition

As an obligate intracellular bacterium and the most common cause of infectious blindness worldwide, the *Chlamydia* genus is comprised of *C. trachomatis*, *C. pneumoniae*, *C. psittaci*, and *C. trachomatis*, responsible for the majority of ocular chlamydial infections, and is further classified into three biovars, ocular (A-C), genital (D-K), and and lymphogranuloma venereum (L1-3), although all immunotypes may cause ocular symptoms. Clinical presentation with trachomatous infection includes a follicular conjunctivitis with conjunctival injection, irritation, and discharge. Characteristic features of trachoma include Herbert's pits, localized depressions following necrosis of limbal follicles; Arlt's line, linear scarring of the upper tarsus; trichiasis, which occurs in late stages of disease; and subsequent secondary corneal opacification. Treatment with tetracyclines or macrolide antibiotics can eliminate the organism.

Cross-References

▶ Conjunctivitis
▶ Follicular Conjunctivitis

Chloasma

▶ Melasma, of Eyelids

Chloasma, of Eyelids

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Synonyms

Melasma

Definition

Dark brown, well-demarcated patches of hyperpigmentation.

Etiology

Common acquired hyperpigmentary disorder with unknown pathogenesis.

Clinical Presentation

Irregular light-to-gray-brown macules seen on sun-exposed areas of the face (cheek, forehead, nose, upper lip, and chin).

Diagnostics

Clinical examination, epidermal pigmentation enhanced with Wood's lamp, biopsy may be performed to determine diagnosis and to determine if dermal hyperpigmentation is present. In vivo reflectance confocal microscopy (RCM) may also be used.

Differential Diagnosis

Nevus, melanoma, pigmentary lesions of the eyelid, and posttraumatic hyperpigmentation.

Therapy

Numerous chemical peeling and hydroquinone- or tretinoin-based creams available.

Prognosis

Lasts longer in darkly pigmented peoples. Epidermal pigmentation may respond to treatment better than dermal involvement.

Epidemiology

More common in women. Associated with oral contraceptive use, chronic atopic eczema, rosacea, or family history.

Cross-References

► Eyelid Inflammation
► Melanin in Eyes

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Chloroquine Toxicity, Cornea Verticillata

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Synonyms

Cornea verticillata; Vertex keratopathy

Definition

Chloroquine toxicity is characterized by whorl-like corneal epithelial deposits.

Etiology

Medications of the chloroquine family, including chloroquine (Nivaquine, Avloclor), hydroxychloroquine (Plaquenil), and amodiaquine, have been associated with keratopathy (Srinivasan et al. 2011). Quinolone antimalarial drugs are used in the prophylaxis and treatment of malaria as well as in the treatment of certain rheumatological disorders (e.g., rheumatoid arthritis, juvenile chronic arthritis, systemic lupus erythematosus). The use of chloroquine has also been advocated in the treatment of calcium abnormalities associated with sarcoidosis (Kanski and Bowling 2011). The use of these drugs have led to multiple ocular manifestations, including vortex keratopathy, decreased corneal sensation, accommodative weakness, posterior subcapsular cataracts, and bull's eye maculopathy (Srinivasan et al. 2011). The corneal deposits in cornea verticillata

associated with chloroquine are composed of unchanged antimalarial salts (Yam and Kwok 2006).

Clinical Presentation

The initial signs of chloroquine toxicity include the development of bilateral, fine gray or golden-brown opacities seen in the inferior corneal epithelium (Kanski and Bowling 2011). The deposits are limited to the corneal epithelium and may vary in pattern (Yam and Kwok 2006). They tend to progress into branching horizontal lines and then into a whorl-like pattern that begins below the pupil, but spares the limbus (Kanski and Bowling 2011). The corneal deposits are concentrated in the central corneal epithelium, with decreased density of deposits in the periphery of the cornea. Corneal deposits are harmless and can develop at doses ranging from 100 mg/day over several years to 1000 mg over only 3 weeks (Srinivasan et al. 2011).

Bilateral keratopathy develops within 2–3 weeks of beginning therapy with chloroquine. While the deposits may involve the visual axis, patients are usually asymptomatic (Srinivasan et al. 2011). Visual acuity is not reduced by corneal deposits secondary to chloroquine (Yam and Kwok 2006). However, they may complain of blurry vision or halos around lights, even without detectable retinopathy or change in visual acuity. Patients may also report diminished corneal sensation with the use of chloroquine (Srinivasan et al. 2011).

Long-term use of antimalarial drugs may lead to disturbances in accommodation on rare occasions. This manifests as an inability to change focus quickly and may occur soon after administration of chloroquine. If the symptoms are bothersome, the dose of chloroquine may be reduced. Another complication of chloroquine toxicity is cataract development. Cataracts have been described in over 20% of patients receiving chloroquine therapy. However, no cataracts have been described in patients receiving hydroxychloroquine. The cataracts associated with chloroquine therapy develop as tiny white flakes axially placed under the posterior lens capsule. The most serious complication of chloroquine therapy is retinal toxicity. Retinal toxicity manifests as a bull's eye maculopathy. Retinal toxicity can affect visual acuity and color vision in its advanced stages (Yam and Kwok 2006).

Diagnosis

Ultrastructural examination reveals concentrically lamellated cytoplasmic inclusions in basal epithelial cells of the conjunctiva and cornea. Confocal microscopy may reveal corneal alterations before they are detectable with slit lamp biomicroscopy. On exam, these patients will have no detectable retinopathy or changes in visual acuity (Srinivasan et al. 2011).

Differential Diagnosis

There are several categories of diseases that may result in crystalline deposits in the cornea:

1. Lipid keratopathies, such as Schnyder's crystalline dystrophy, Tangier disease, and familial lipoprotein disorders
2. Errors of protein metabolism, such as tyrosinemia, cystinosis, hyperuricemia, and gout
3. Acquired immunoprotein keratopathies, such as multiple myeloma, cryoglobulinemia, benign monoclonal gammopathy, and rheumatoid arthritis
4. Infectious crystalline keratopathies
5. Miscellaneous dystrophies and metabolic abnormalities, such as posterior crystalline corneal dystrophy, Bietti's corneal dystrophy, porphyria, and calcium deposition
6. Drug deposition, such as chrysiasis, chlorpromazine, and chloroquine deposits

The diagnosis can be differentiated based upon histopathology of the crystalline deposits, clinical appearance of the deposits, and systemic evaluation (Grimmett 2011).

Prophylaxis

The hydroxychloroquine dose for therapy has decreased over the past thirty years, resulting in a decreased incidence of corneal toxicity (Yam and Kwok 2006).

Therapy

Corneal deposits are completely reversible with discontinuation of the offending chloroquine derivative. Regardless of the duration of chloroquine exposure, no residual corneal damage ensues. The development of corneal toxicity is not an indication to discontinue therapy. However, these patients should be carefully evaluated for maculopathy, which is a serious complication of chloroquine toxicity and would be an indication for discontinuation of the drug (Yam and Kwok 2006).

Prognosis

The development of keratopathy has no correlation with the dose or duration of therapy with quinolone medications. Discontinuation of quinolone drugs typically results in gradual elimination of the subepithelial deposits. They may clear despite continued therapy with the implicated drug (Kanski and Bowling 2011). Thus, development of keratopathy is not an indication for discontinuing therapy. However, the development of keratopathy is associated with an increased incidence of chloroquine-associated retinopathy (Srinivasan et al. 2011).

Epidemiology

Bilateral keratopathy affects 28–95% of patients on treatment with chloroquine. Hydroxychloroquine has a decreased incidence of bilateral keratopathy compared to chloroquine, approximating 1–28% (Srinivasan et al. 2011). This difference may reflect a lower degree of hydroxychloroquine accumulation in the cornea compared to chloroquine or differing tendencies of the two drugs to bind to corneal tissue (Yam and Kwok 2006).

Cross-References

- ▶ Fundus Salt and Pepper
- ▶ Nyctalopia: Night Blindness

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Chlorpromazine Keratopathy

▶ Chlorpromazine, Cornea Verticillata

Chlorpromazine Retinopathy

▶ Chlorpromazine, Retinal Degeneration

Chlorpromazine, Cornea Verticillata

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Synonyms

Chlorpromazine keratopathy

Definition

Chlorpromazine is a sedating antipsychotic medication that with long-term use can result in corneal verticillata, or whorls.

Etiology

Chrysiasis generally results from medical treatment of disorders such as rheumatoid arthritis with injection or oral therapy with gold.

Clinical Presentation

Patients may present with subtle, diffuse yellowish-brown granular deposits in the posterior stroma, Descemet membrane, and endothelium. These deposits generally only occur in the exposed cornea of the interpalpebral fissure. Patients may also develop fine, stellate yellowish-brown deposits on the anterior lens capsule. In the retina, chlorpromazine usage may result in a pigmentary granularity and clumping.

Diagnosis

Chlorpromazine verticillata would be diagnosed with careful examination of the cornea under slit-lamp examination.

Differential Diagnosis

Other causes of a vortex keratopathy include chloroquine, hydroxychloroquine, amiodarone, silver, gold, and amantadine toxicity.

Prophylaxis

Preventing ingestion of chlorpromazine would prevent this process from occurring.

Therapy

Chlorpromazine verticillata is visually asymptomatic; there is no therapy for this entity.

Prognosis

Prognosis is good as chlorpromazine verticillata will remain visually asymptomatic requiring no treatment. In some cases, the depositions may clear after the cessation of therapy, while in others the depositions never disappear.

Epidemiology

Chlorpromazine verticillata occur after long-term ingestion of chlorpromazine. Lens deposits occur in 50% of patient who ingest over 1,000 g of the drug. The normal daily dose of chlorpromazine is 75–300 mg.

Cross-References

▶ Chrysiasis, Corneal Pigmentation

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Chlorpromazine, Retinal Degeneration

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Synonyms

Chlorpromazine retinopathy; Phenothiazine retinopathy; Thorazine-induced retinal degeneration; Thorazine retinopathy

Definition

Chlorpromazine-induced pigmentary retinopathy.

Etiology

Phenothiazines are a group of tranquilizing drugs with antipsychotic actions that are thought to act by blocking synaptic transmission of the neurotransmitter dopamine within the brain. Chlorpromazine (Thorazine) and thioridazine (Mellaril), phenothiazine drugs commonly used for schizophrenia and other psychotic disorders, are known to be associated with several adverse effects, including ocular and dermatological complications (Yanoff and Duker 2008). These drugs can bind to melanin granules in the uveal tissue and when used in high dosages can cause abnormal pigmentation of the eyelids, conjunctiva, cornea, and lens (Regillo 2012). These side effects usually do not cause visual impairment (Agarwal 2012) and are at least partially reversible upon cessation of the drugs (Chern and Saidel 2011).

A more serious and vision-threatening complication of phenothiazine medications involves the cone and rod photoreceptors in the neurosensory retina and the retinal pigment epithelial (RPE) cells. Most cases have been reported in association with thioridazine and chlorpromazine use (Chern and Saidel 2011). It is possible that retinal functions mediated by the neurotransmitter dopamine are being compromised by phenothiazines, leading to formation of retinal abnormalities. Further, these drugs are photosensitizers and can produce light-induced damage to cells and tissues, with resultant pigmentary retinopathy and outer retinal degeneration (Ryan 2012). In contrast to thioridazine which may cause severe subacute retinopathy after a few weeks of dosages above 800 mg/day (standard dose range 150–600 mg/day), chlorpromazine retinopathy is typically milder and is seen at higher dosages of 2,400 mg/day (standard dose range 75–300 mg/day) taken throughout months to years (Chern and Saidel 2011).

Clinical Presentation

The early pigmentary changes in the retina are rarely associated with visual or functional deficits. Massive doses of chlorpromazine may lead to peripheral visual field loss, night blindness (nyctalopia), color vision disorders (dyschromatopsia), and, eventually, loss of central vision (Chern and Saidel 2011). Initially, the fundus examination may be normal, and a high index of suspicion may be needed before coarse RPE stippling in the posterior pole and other pigmentary abnormalities become evident. Further toxicity may lead to retinal granularity, pigment clumping, and widespread but patchy atrophy of the RPE and choriocapillaris, with a characteristic nummular pattern of involvement extending centrally from the peripheral retina. It has been reported that chlorpromazine-associated pigmentary retinopathy is usually irreversible even with cessation of the drug (Yannof and Duker 2008).

Diagnosis

Obtaining extended anamnestic data is paramount in order to identify chlorpromazine or other phenothiazine drug as the cause of the patient's complaints. Clinical observation, photographic documentation, and periodic follow-up to assess recovery or progression are warranted. Visual field changes are nonspecific, and most characteristically show paracentral scotomas or peripheral ring scotomas. Intravenous fluorescein angiography may reveal a wide spectrum of RPE abnormalities ranging from mild alterations to extensive areas of window defects and staining consistent with atrophy of the RPE and choriocapillaris. Though in early phases of the disease electroretinographic (ERG) testing may be within normal limits, an attenuated ERG is an indication of severe toxicity (Chern and Saidel 2011).

Differential Diagnosis

Because patients receiving chlorpromazine have often received other medications that may have

included potentially retinotoxic drugs, assignment of the exact cause of the retinopathy may be difficult.

Differential diagnosis includes pigmentary retinopathy associated with other phenothiazine medications, inherited retinal degenerations such as retinitis pigmentosa, and cancer-associated retinopathy (Chern and Saidel 2011).

Prophylaxis

The deleterious effects of thioridazine appear much sooner than those of other phenothiazines, but chlorpromazine-associated adverse effects are also related to the dose and duration of the treatment. Patients using chlorpromazine are generally not monitored with routine ophthalmoscopy because toxicity is rare at standard doses. However, suspected cases or patients who have taken the drug at high doses should undergo full ocular evaluation and regular monitoring, as toxic side effects of progressive phenothiazine-induced retinopathy can ensue within weeks. Subsequently, atrophy of the RPE can become manifest, and severe visual loss can occur (Yanoff and Duker 2008).

Therapy

Immediate discontinuation of phenothiazine and periodic ocular assessments should be performed, including examinations to document recovery or progression after cessation of the drug (Chern and Saidel 2011).

Prognosis

In cases of early toxicity, immediate cessation of medication may result in reversal of both the functional visual and morphological abnormalities. In most cases, despite slow improvement in visual function, the pigmentary changes of the RPE are irreversible. In some cases, however, the severity of retinopathy may progress, and visual the deterioration may actually continue despite cessation of the medication. It is not known whether these late atrophic changes after discontinuation of the drug represent continued toxicity or a decompensation of cells that were injured when the drugs were used initially (Chern and Saidel 2011).

Epidemiology

Even though chlorpromazine and thioridazine have been largely replaced by newer antipsychotic drugs, awareness to their potential side effects is warranted, and cautious periodic observation of patients treated with these medications is recommended to lessen the frequency of phenothiazine-induced serious visual loss. Of note, the massive doses which were once given and led to these findings are rarely prescribed currently. As such, chlorpromazine-induced retinal toxicity is becoming an extremely rare entity (Agarwal 2012).

Cross-References

- ▶ Altitudinal Visual Field Defects
- ▶ Atypical Retinitis Pigmentosa (RP)
- ▶ Cancer-Associated Retinopathy
- ▶ Electroretinogram
- ▶ Inherited Color Vision Disorders
- ▶ Multiple Recurrent Serosanguineous Retinal Pigment Epithelial Detachments in Black Women
- ▶ Nyctalopia: Night Blindness

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Chocolate Cyst

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Synonyms

Lymphangioma

Definition

The term chocolate cyst refers to a blood-filled cystoid space and is so named due to the dark red-brown appearance of such a lesion. These appear in multiple organ systems; however, in the orbit, it is classically associated with hemorrhage in orbital lymphangioma, which may cause a rapid increase in size.

Cross-References

► Vascular Tumors Disease of the Conjunctiva

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Cholestasis with Peripheral Pulmonary Stenosis

► Arteriohepatic Dysplasia (Alagille Syndrome), Retinal Degeneration

Cholesterol Emboli (Hollenhorst Plaques)

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Small, solitary or multiple, discrete oval or rhomboid-shaped, bright, refractile, yellowish plaques lodged in the lumen of retinal arteriolar bifurcations, usually originating from atheromatous plaque within the carotid arteries. They may indicate severe atherosclerosis and previous ischemic episode in the eye.

Retinal cholesterol emboli can cause a visual field defect when they block the vascular flow or remain asymptomatic. They may move in the arterioles and finally disappear. They can be associated with the rare entity – cholesterol crystal embolism.

Retinal cholesterol emboli are called also Hollenhorst plaques after the American ophthalmologist Dr. Robert Hollenhorst (1913–2008) who first described their significance in 1961.

Chorioretinal Coloboma

► Ectasia, Retinal

Choristoma

► Epidermoid Cysts

Choristomas

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Synonyms

Ectopic lacrimal gland; Epibulbar osseous choristoma; Limbal or epibulbar dermoid

Definition

A choristoma is defined as a group of histologically normal cells in an abnormal location. A simple choristoma consists of one type of tissue, whereas a complex choristoma is comprised of multiple types of tissues.

Etiology

Epibulbar choristomas are thought to occur as congenital anomalies in utero at 5–10 weeks gestation. The exact pathogenesis is not clearly understood. Limbal dermoids are not typically inherited except in the case of Goldenhar's syndrome, where inheritance patterns are variable, and ring dermoid syndrome, where inheritance is autosomal dominant.

Clinical Presentation

Choristomas of the anterior segment are comprised of the skin, bone, lacrimal gland, and/or cartilage.

Limbal or epibulbar dermoids typically present in the inferotemporal cornea and conjunctival epibulbar regions as tan or white elevated masses. They can range from very small, minimal growths to large protuberant masses. They often have protruding hairs. A yellow white lipid demarcation line may be seen in the corneal stroma.

Rarely, limbal dermoids present bilaterally as 360 conjunctivoscleral rings around the cornea, such as seen with ring dermoid syndrome.

Mann's grading system for limbal dermoids stratifies lesions into one of three grades based on anatomic involvement. Grade one lesions are the most common and consistent of epibulbar limbal lesions with superficial corneal involvement. Grade two lesions affect the full-thickness cornea, with potential Descemet's and endothelial sparing. Grade three lesions involve the entire cornea and all anterior chamber structures. The latter are the most rare.

Ectopic lacrimal gland choristomas tend to present as vascularized, pink nodules in the perilimbal region. These ectopic lacrimal glands are thought to represent the ectopic palpebral lobe due to the presence of smooth muscle on histopathologic examination. Care must be taken to distinguish a true ectopic lacrimal gland choristoma from a prolapsed lacrimal gland, because excision of the latter would result in permanent dry eye. Ectopic lacrimal glands usually extend deep into the cornea and sclera and may only be partially excised. They have been associated with encephalocraniocutaneous lipomatosis.

Epibulbar osseous choristomas are the least common type of choristoma and tend to appear as fleshy yellow subconjunctival nodules in the supertemporal quadrant. They seldom involve the cornea, are well circumscribed, and are usually located 5–10 mm behind the limbus. These lesions are comprised of compact bony tissue. Epibulbar osseous choristomas not demonstrate growth.

All of these lesions are present at birth, but tend to be detected in the first or second decade of life. There is no racial or sexual predilection for developing them. Choristomas may or may not be associated with systemic conditions such as Goldenhar's syndrome and epidermal nevus syndrome.

Diagnosis

Clinical, biopsy.

Differential Diagnosis

The differential diagnosis of a limbal dermoid includes epidermal cyst, foreign body granuloma, atypical pterygium, sclerocornea, Peter's anomaly, juvenile xanthogranuloma, and hemangioma. The differential diagnosis of a dermolipoma includes prolapsed orbital fat, lymphoma, or a herniated lacrimal gland. The differential diagnosis of an osseous choristoma includes prolapsed orbital fat and extraorbital tumor extension.

Therapy

Therapy involves observation, lubrication if ocular irritation occurs, or surgical resection if lesions induce astigmatism and amblyopia or are cosmetically unacceptable. Surgery may involve lamellar sclerectomy, sclerokeratectomy, or penetrating keratoplasty depending on the location of the lesion. Amniotic membrane may be used to cover conjunctival defects. All remnants of dermoids and dermolipomas should be meticulously excised because residual material may cause a large inflammatory response. Total excision is particularly difficult to accomplish with dermolipomas, because these choristomas usually extend into the fornices and become enmeshed with orbital fat and extraocular muscles.

Complications of surgical resection include extraocular motility limitation from scarring, worsening astigmatism, and globe penetration.

Prognosis

The overall prognosis is good. These congenital lesions tend to have limited postnatal growth which mirrors the patient's growth. They do not undergo malignant transformation. If the lesions are large and straddle the cornea, prognosis is less favorable due to the likelihood of induced astigmatism and amblyopia.

Epidemiology

Worldwide incidence of limbal dermoids is estimated to be 1–3 per 10,000. Dermolipoma tends to be the most common epibulbar choristoma, followed by dermoid.

C

Cross-References

▶ Conjunctival Tumors
▶ Goldenhar Syndrome

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Choroid, Gyrate Atrophy of

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Synonyms

Gyrate atrophy of the retina and choroid; Hyperornithinemia with gyrate atrophy (HOGA); Ornithine aminotransferase (OAT) deficiency

Definition

Gyrate atrophy is an autosomal recessive, slowly progressive chorioretinal dystrophy caused by mutations in the gene encoding ornithine

aminotransferase. Patients generally start to notice nyctalopia and peripheral field loss in the second to fourth decades of life. This eventually evolves into tunnel vision and ultimately central vision loss. Considerable variability exists in age of first symptoms, legal blindness, and loss of central vision. Patients characteristically will have elevated serum ornithine levels 10–20 times normal, hyperornithinuria, and hypolysinemia due to a deficiency in ornithine aminotransferase.

Clinical exam shows bilateral distinct circular areas of chorioretinal atrophy in the retinal periphery and mid-periphery. With time, these lesions coalesce into larger areas of chorioretinal atrophy with scalloped edges and eventually progress to involve the macular region. Pigmentation in and around the lesions can also be present. Patients may also be myopic and posterior subcapsular cataracts are common. Visual field testing confirms restriction in peripheral fields. Full-field electroretinogram (ERG) shows severe reduction in rod and cone responses that eventually become non-detectable with time.

Ornithine aminotransferase is an enzyme localized to the mitochondria matrix in most tissues. Systemic findings can be seen with gyrate atrophy, but most of these changes are subclinical and asymptomatic. Systemic changes include thinning of hair, subclinical proximal skeletal muscle atrophy, abnormal electroencephalogram (EEG), abnormal electrocardiogram (ECG), and MRI findings of premature atrophy and white matter changes in the brain.

No treatment currently exists to halt or reverse the ocular changes seen with gyrate atrophy. Diet supplementation with vitamin B6 and/or diets low in arginine, the precursor to ornithine, may slow disease progression.

Etiology

Gyrate atrophy is caused by mutations occurring in the ornithine aminotransferase gene on chromosome 10q26. This gene encodes the vitamin B6-dependent mitochondrial enzyme, ornithine aminotransferase, which converts ornithine to glutamate and proline. Significant heterogeneity exists with more than 60 different known mutations.

Occurrence

Gyrate atrophy is a rare autosomal recessive disease. Males and females are equally affected. Patients from Finland, Western Europe, Israel, Japan, and the United States have been reported in the literature.

Classification

Two different subtypes of gyrate atrophy exist, likely due to variation in the genotypic mutations. These subtypes are distinguished by response to treatment with supplementation of vitamin B6, a cofactor necessary for normal ornithine metabolism. Those that respond to vitamin B6 supplementation have a significant drop in serum ornithine levels to near normal levels. Nonresponsiveness to vitamin B6 supplementation is more common. These patients may benefit by a low arginine diet to lower serum ornithine levels. However, the effect of dietary changes on progression of ocular disease is variable and again may be due to the heterogeneity of mutations causing gyrate atrophy.

Cross-References

► Nyctalopia: Night Blindness

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Choroidal and/or Ciliary Body and/or Iris Melanoma

► Uveal Melanoma

Choroidal Coloboma

► Ectasia, Retinal

Choroidal Hemangioma

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Definition

A benign vascular hamartoma of the choroid. (Iris and ciliary body hemangiomas are extremely rare.)

Etiology

Circumscribed choroidal hemangioma (CCH) is a hamartoma. It occurs sporadically without any associated ocular or systemic anomalies. There is no evidence of genetic etiology. It is composed of vascular spaces lined by endothelial cells and involves the full thickness of the choroid.

Clinical Presentation

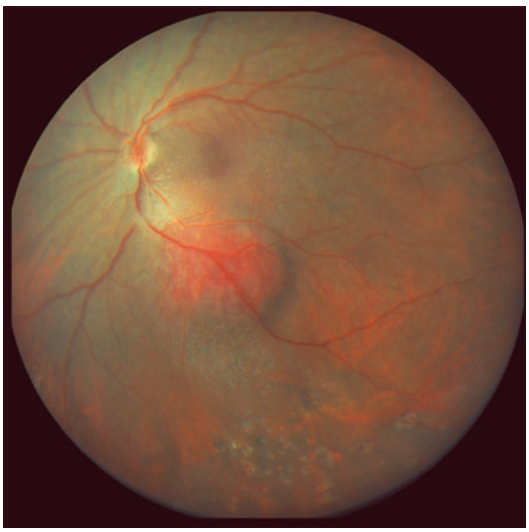
CCH appears ophthalmoscopically as a red-orange choroidal mass with indistinct margins that blend with the surrounding choroid. It is usually located in the posterior choroid, in the proximity of the optic nerve head or temporal to it, with no evident intrinsic tumor vessels or feeder vessels. CCH becomes symptomatic not before the third decade of life. Symptoms are due to associated subretinal fluid/exudative retinal detachment or cystoid macular edema that cause decreased visual acuity or other visual disturbances such as metamorphopsia. The presence of the tumor mass itself can also affect visual acuity (Naseripour and Singh 2014).

Diagnostics

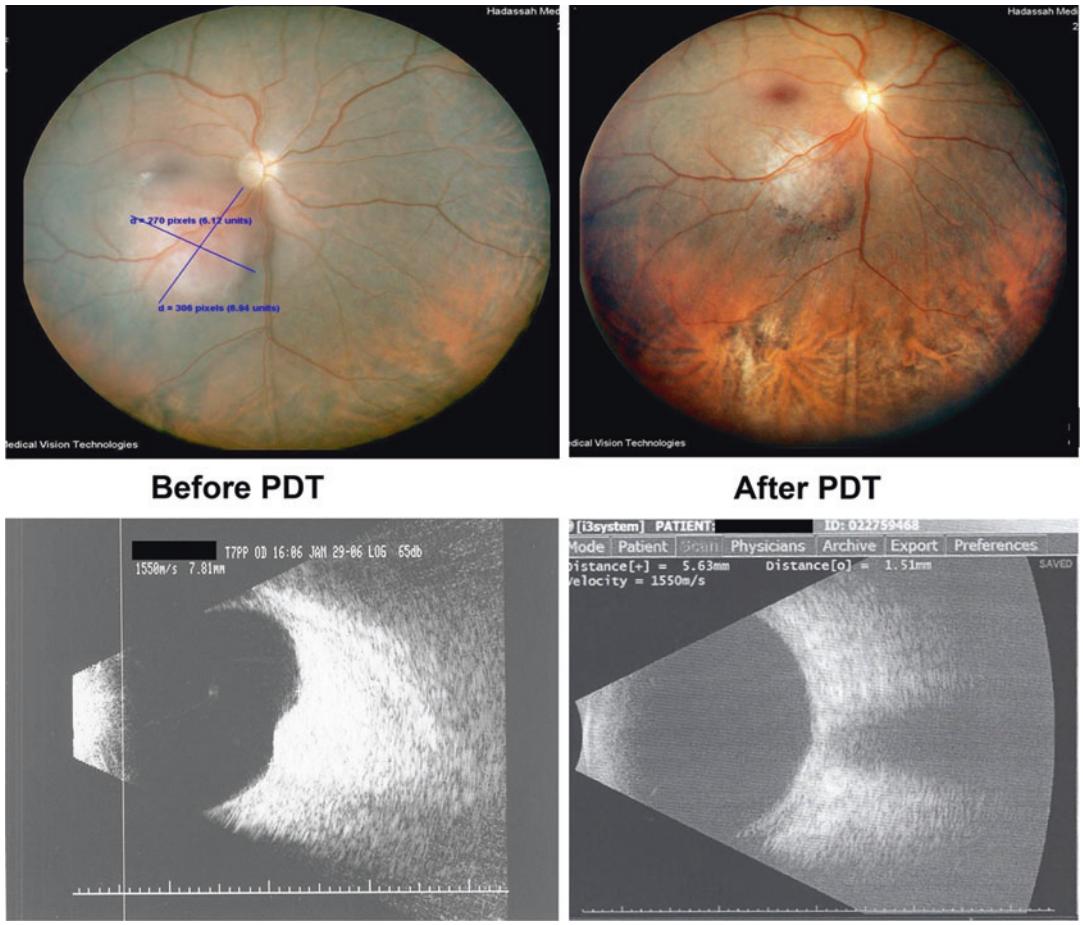
The clinical features of CCH are essential for the diagnosis of CCH and should be documented by fundus photography. Ultrasonographic and angiographic studies are helpful in establishing the correct diagnosis. By B-scan ultrasonography CCH appears as a dome-shaped choroidal mass with a smooth contour, and A-scan demonstrates high internal reflectivity. On fluorescein angiography, the CCH shows early hyperfluorescence that increases with lacy network of intrinsic vessels. These intrinsic vascular patterns are better displayed with indocyanine green (ICG) angiography. Optical coherence tomography is used to show the retinal changes over and around the CCH.

Differential Diagnosis

Differential diagnosis includes → amelanotic choroidal melanoma → choroidal metastasis →



Choroidal Hemangioma, Fig. 1 A red-orange choroidal hemangioma with indistinct borders under the lower temporal retinal vascular arcade



Choroidal Hemangioma, Fig. 2 Fundus and ultrasound pictures of choroidal hemangioma touching the inferior-temporal margin of the optic nerve head before treatment (*left*) and after treatment by PDT (*right*)

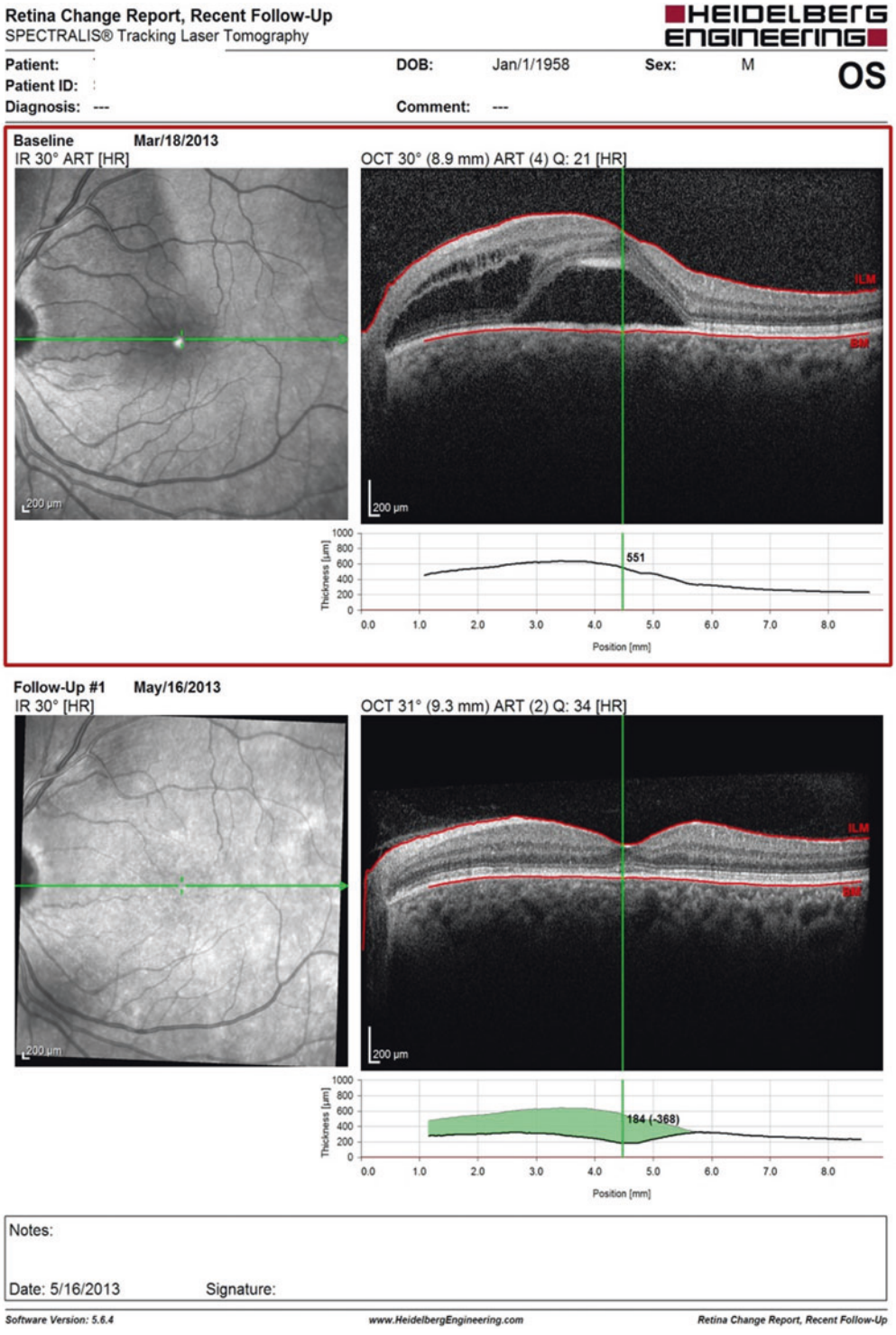
posterior scleritis → choroidal granuloma → atypical central serous retinopathy.

Prophylaxis

None. Asymptomatic CCH should be followed for early changes that can lead to visual disturbances.

Therapy

Asymptomatic CCH does not need treatment and should be observed. Symptomatic CCH must be treated in order to preserve vision. Radiation therapy, usually of low dose, has been applied in treating CCH via various methods: external beam radiotherapy, episcleral plaque brachytherapy (Co-60, Ru-106, I-125, Pd-103), proton beam radiotherapy, and stereotactic and gamma knife radiosurgery. Transpupillary thermotherapy (TTT) has been used, but because of visually significant complications it is not suitable for CCH located in the subfoveal or juxtapapillary regions. Photodynamic therapy (PDT) using verteporfin has been proven to be a very effective method and is currently the most popular way of treating CCH. It can be applied using the standard protocol (which is used in



Choroidal Hemangioma, Fig. 3 Optical coherence tomography of the retina in an eye with choroidal hemangioma located superior to the optic nerve head, showing subretinal and intraretinal fluid in the macular area (*above*), returning to normal after treatment of the hemangioma by PDT (*below*)

treating AMD), but modified protocols have been used (Schmidt-Erfurth et al. 2002). Intravitreal injections of anti-VEGF drugs (bevacizumab and ranibizumab) with or without PDT or TTT and oral propranolol have been used for reducing subretinal and intraretinal fluid.

Prognosis

CCH is a benign lesion that does not threaten life. Visual loss caused mainly by subretinal and intraretinal fluid can improve with treatment. However, when treatment is late or when the macula or papillomacular area is involved, the long-term prognosis for vision is poor. The use of PDT in recent years has improved the visual prognosis (Figs. 1, 2, and 3) (Shields et al. 2001).

Epidemiology

CCH is rare and no epidemiological data are available.

Cross-References

- ▶ Choroidal and/or Ciliary Body and/or Iris Melanoma
- ▶ Scleritis

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Choroidal Neovascularization

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Definition

Choroidal neovascularization (CNV) is defined as the pathological growth of new blood vessels that originate from preexisting choroidal vessels and proliferate in either the subretinal (between the retina and RPE) or subretinal pigment epithelial (between Bruch's membrane and the RPE) space via a break in Bruch's membrane. This process is commonly associated with severe visual loss and may eventually lead to blindness.

Classification

Choroidal neovascularization is generally classified into two main categories depending on the location of the new blood vessel growth. Proliferation in classic CNV occurs in the subretinal space, whereas occult CNV is characterized by the proliferation of blood vessels under the RPE. In classic CNV there are typically one or few breaks in the Bruch's membrane, and the vessels then proliferate in the subretinal space. Occult CNV, on the other hand, tends to occur with multiple breaks in Bruch's membrane and thus multiple growth sites. The vessels tend to grow laterally under the RPE between lipids accumulated in Bruch's membrane and the basal laminar deposits (Grossniklaus and Green 2004). There can also be CNV that is a combination of these two types.

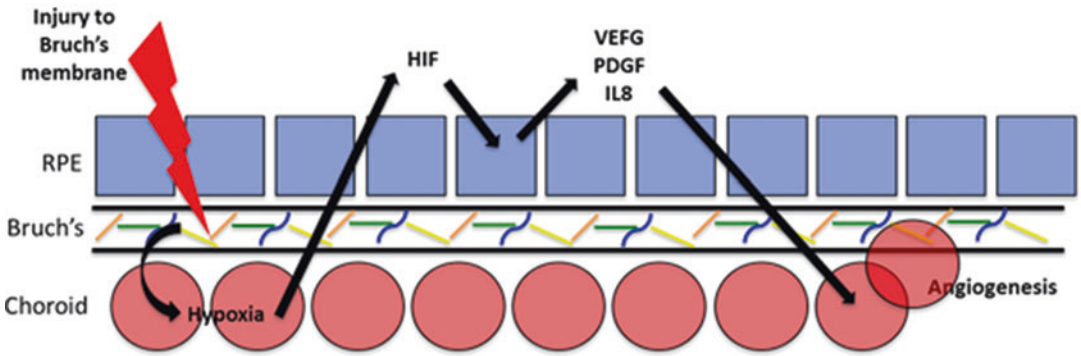
Etiology

Pathogenesis

The development of CNV is a dynamic process which may develop secondary to virtually any form of injury or inflammation at or around Bruch's membrane or the RPE. Bruch's membrane plays an important role in choroidal homeostasis, RPE attachment, and transport of nutrients and waste products between the RPE and choroid (Gliem et al. 2014). It also serves as a physical barrier between the choroid and the RPE and thus prevents the invasion of vessels. Once the disease process is initiated with injury to Bruch's membrane, the choroid becomes hypoxic and releases hypoxia inducible factor (HIF) (D'Ambrosio et al. 2014). The release of HIF then leads to the production of several angiogenic and inflammatory factors by the retinal photoreceptors and RPE which in turn disrupts the normal balance of these factors and thus leads to inflammation and neovascularization (Fig. 1).

These angiogenic and inflammatory factors include vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), as well as the inflammatory cytokine IL8 which are produced by retinal photoreceptors and the RPE (Grossniklaus and Green 2004). It has also been found that macrophages accumulate around breaks in Bruch's membrane and produce TNFα which then stimulates further production of VEGF, PDGF, and IL8 (Grossniklaus and Green 2004). The concentration of VEGF is the highest near Bruch's membrane which allows vascular endothelial proliferation to and through the membrane (D'Ambrosio et al. 2014). PDGF allows for stabilization and maturation of the new vessels by allowing pericytes to coat the endothelial cells (Kaiser 2013). IL8 causes inflammation that increases the permeability of the new vessels and allows leakage of serum into the subretinal or sub-RPE space. The macrophages found near the breaks in Bruch's membrane also produce tissue factor (TF) and matrix metalloproteinases (MMPs). TF causes fibrogenesis and the formation of a scaffold onto which the newly formed blood vessels can grow and proliferate (Grossniklaus and Green 2004). The MMPs digest tissue in the eye and allow for neovascularization to occur in and through the different planes in the eye. The combination of angiogenesis and edema in the subretinal or sub-RPE space causes damage to the RPE and photoreceptors and thus can result in focal retinal detachment and vision loss (van Lookeren Campagne et al. 2014).

As CNV progresses, the retinal photoreceptors and RPE increase production of anti-inflammatory



Choroidal Neovascularization, Fig. 1 Injury to Bruch's membrane leads to hypoxia of the choroid and its release of HIF followed by release of angiogenic and inflammatory factors from the RPE which thus causes neovascularization

and anti-angiogenic factors. Specifically TGF-β is released in increasing amounts throughout the process (Grossniklaus and Green 2004). Eventually, there is enough TGF-β to fully inhibit the inflammation and angiogenesis in CNV. Continued activity of the disease leads to proliferation of RPE cells, fibroblasts, and glial cells which leads to the formation of fibrovascular scar tissue known as a disciform scar in the subretinal or sub-RPE space (Grossniklaus and Green 2004).

Risk Factors/Underlying Disease

The etiology of CNV varies widely with age. In the younger population, traumatic damage to Bruch's membrane is most common. In individuals older than 50 years of age, however, age-related macular degeneration (ARMD) is typically seen. Inflammatory diseases and pathologic myopia may lead to CNV in any age group (Yanoff & Duker: Ophthalmology 2008).

The most common etiology of CNV is ARMD (Cohen et al. 1996). ARMD is a progressive degenerative disease that increases in frequency with age. The most severe manifestation of ARMD is CNV. It is hypothesized that injury to Bruch's membrane occurs secondary to oxidative damage and drusen (lipid and protein waste droplets) deposition. Oxidative damage leads to an increase in VEGF production and therefore causes an imbalance between angiogenic and anti-angiogenic factors which leads to new vessel formation (van Lookeren Campagne et al. 2014).

ARMD is the most common etiology in the elderly; however, in patients less than 50 years old, pathologic myopia is the most common cause. Patients with pathologic myopia have refractive errors of −6 diopters or more. Fractures of Bruch's membrane, commonly known as lacquer cracks, are commonly found in these patients. They have been shown to be a predisposing factor for the development of CNV. The fundus may also show peripapillary chorioretinal atrophy, gyrate atrophy of the RPE, or a posterior staphyloma which may lead to damage to Bruch's membrane and development of CNV (Cohen et al. 1996).

Other, rarer diseases may lead to the development of CNV. Infectious causes include ocular histoplasmosis syndrome (OHS) in which infection of the eye with *Histoplasma capsulatum* leads to antigen deposition in Bruch's membrane. A reactive inflammatory response to the antigen deposition causes a break in the membrane and the initiation of the development of CNV (Grossniklaus and Green 2004).

Certain genetic factors may also predispose patients to CNV. Pseudoxanthoma elasticum, a genetic disease with an autosomal recessive mutation of adenosine triphosphate-binding cassette subfamily C member 6 (ABCC6) gene, may manifest as thickening and calcification of Bruch's membrane. These alterations in Bruch's membrane cause thinning of the choroid which leads to hypoxia and release of HIF (Gliem et al. 2014). Similarly, pathological myopia is also inherited as an autosomal recessive disorder in many cases. Ocular histoplasmosis syndrome is also more frequently seen in HLA-B27 and HLA-DR2. CNV may also manifest as an uncommon complication of uveitis, especially posterior uveitis (D'Ambrosio et al. 2014).

Idiopathic CNV is defined as CNV in individuals less than 50 years old that do not have any evidence of trauma, pathological myopia, or any other intraocular inflammation.

Clinical Presentation

The presentation of CNV varies from patient to patient and may be found before the patient complains of severe symptoms. The most common presentations of CNV include metamorphopsia (distorted vision) and central scotomas. Patients will also complain of decreased visual acuity. Importantly, patients with CNV will not complain of any eye pain (Wong et al. 2014).

Diagnosis

Clinical Exam

When a patient presents with symptoms of metamorphopsia and central scotomas, it is important to keep CNV high on the differential diagnosis list. On slit-lamp biomicroscopy, fundus changes can be seen. Retinal changes may include

localized elevation due to detachment of the RPE and retinal edema. The macula may show gray-green discoloration, and exudates may be present in or around the macula. Subretinal hemorrhage may also be visible.

Fluorescein Angiography (FA)

Fluorescein angiography (FA) is used to diagnose and classify CNV. Two major patterns of CNV are seen: classic and occult CNV.

Classic CNV

Classic CNV is characterized by hyperfluorescence initially after injecting the dye followed by progressive leakage throughout the course of the angiogram. This pattern is seen in only 10% of patients with CNV due to ARMD but is seen more frequently in other causes of CNV (Wong et al. 2014; Bressler 2012).

Occult CNV

Occult CNV can be further subdivided into two types:

1. Fibrovascular pigment epithelial detachment (PED): vessel and fibrous tissue infiltration leads to RPE elevation and thus a fibrovascular PED. In this type, fluorescence within the fibrous PED slowly increases after injection of the dye followed by a unique staining pattern late in the angiogram.
2. Late leakage from an undetermined source: lack of fluorescence early in the angiogram is followed by areas of fluorescence seen later during the test.

CNV lesions are described based on the proportion of classic component in the CNV lesion. Predominantly classic lesions are described as having more than 50% classic component in the lesion, minimally classic lesions are described as having between 1% and 49% of classic component, whereas occult with no classic CNV suggests there is no classic component in the CNV lesion.

Identification of classic and occult components used to be critical in the management of CNV, since treatment strategies such as photodynamic therapy (PDT) and focal laser treatment varied depending on the portion of classic CNV. However more recently, the use of anti-VEGF treatment agents has reduced the need for this distinction since treatment doesn't change based on this criterion.

Optical Coherence Tomography (OCT)

OCT plays a critical role in evaluating the progression of CNV and response to treatment in patients with CNV (Cavalcante et al. 2014). OCT provides high-resolution images of posterior eye structures and can demonstrate vascular activity. Frequently seen findings in such patients include intraretinal and subretinal fluid, intraretinal cystic spaces, RPE elevation, neurosensory detachment, and intraretinal hyperreflective flecks (Giani et al. 2011).

Fundus Photography

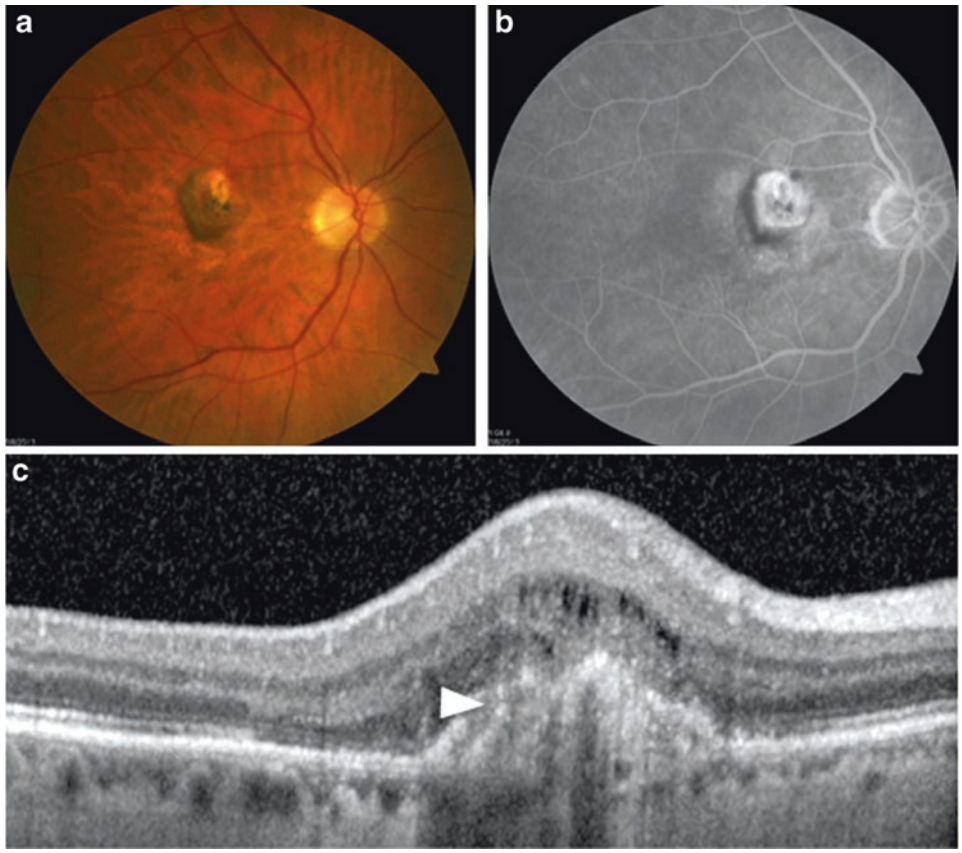
Fundus photography can be used as an adjunct when diagnosing and classifying CNV. It may also help determine the underlying cause of CNV. Color fundus photography allows visualization of the macula and the retina. It can show subretinal hemorrhages, geographic atrophy, exudates, and blood vessels. Fundus photography is not used in every patient to diagnose CNV (Fig. 2).

Differential Diagnosis

The symptoms of metamorphopsia and central scotomas are found in most patients with CNV; however, it is important to exclude other pathology. Other conditions that may present like CNV include angioid streaks, central serous chorioretinopathy, and macular edema.

Prophylaxis

The AREDS trial was a randomized multicenter clinical trial that evaluated the effect of high-dose vitamin regimens on the progression of AMD. It was shown that in patients with intermediate AMD a combination of both antioxidants (500 mg vitamin C, 400 IU vitamin E, and



Choroidal Neovascularization, Fig. 2 A 67-year-old patient with neovascular AMD. (**a**) Color fundus photograph shows a *greenish brown* lesion, approximately one disk diameter in size within the macula. (**b**) Fluorescein angiogram showing hyperfluorescence of the lesion. (**c**) Optical coherence tomogram of the same patient showing a hyperreflective neovascular lesion (*arrow head*) disrupting the RPE-choriocapillaris complex with accompanying intraretinal fluid

15 mg β-carotene) and zinc (80 mg zinc oxide plus 2 mg copper) leads to a 25% reduction in progression to advanced AMD and a 19% reduction in rates of moderate visual loss. Patients without AMD or in the early stages of AMD did not seem to benefit from this formulation. Antioxidants or zinc alone, however, were not shown to prevent the progression of AMD (Eter et al. 2006).

This trial was followed up by the AREDS2 trial in which beta-carotene was substituted with lutein and zeaxanthin, since beta-carotene had previously been associated with increased risk of lung cancer in previous smokers. Omega-3 fatty acids were also added to the formulation. The study found that while omega-3 fatty acids had no effect on the formulation, lutein and zeaxanthin appeared to be a safe replacement to beta-carotene (Eter et al. 2006).

Therapy

Laser Photocoagulation

The first surgical treatment of CNV was laser photocoagulation. The principle behind laser treatment was to cauterize the feeder vessels of subfoveal CNV to prevent further hemorrhage and edema (Hanout et al. 2013). In the Macular Photocoagulation Study (MPS) it was shown that severe visual loss was significantly decreased in treated eyes. Although visual loss was decreased,

patients who were treated had an increased risk of vision loss during the early stages of the treatment. Therefore, laser photocoagulation is no longer recommended for the treatment of subfoveal CNV (Hanout et al. 2013).

Verteporfin Photodynamic Therapy (PDT)

Verteporfin photodynamic therapy uses light-activated verteporfin to induce occlusion of new vessels (Hanout et al. 2013). Patients treated with PDT demonstrated better visual acuity benefits compared with the placebo after 12 months of treatment. The response to treatment was not stable after 24 months (Wolf et al. 2014). PDT was thus used to help prevent visual acuity loss while other treatments were being developed.

Anti-VEGF Agents

Pegaptanib Sodium Pegaptanib sodium is an aptamer that binds specifically to VEGF165, the most prevalent isoform in neovascular AMD, to block its activity and therefore prevent the proliferation of new vessels (Eter et al. 2006; Hanout et al. 2013; Bressler 2009). The VISION trial was a randomized controlled trial that studied the efficacy of intravitreal pegaptanib intravitreal injections for the treatment of CNV (Eter et al. 2006). Three different doses (0.3, 1.0, and 3.0 mg) given at 6-week intervals for a total of 48 weeks were compared to a sham treatment (Bressler 2009). All doses were shown to stabilize visual acuity in patients with all types of CNV after 1 year of treatment and beyond if treatment is continued (Eter et al. 2006). The side effects of pegaptanib sodium included eye pain, vitreous floaters, punctate keratitis, increased intraocular pressure, endophthalmitis, retinal detachment, and traumatic cataract (Eter et al. 2006; Hanout et al. 2013). Pegaptanib was thus approved by the US Food and Drug Administration (FDA) as a treatment for CNV in December 2004.

Ranibizumab Ranibizumab is the antigen binding fragment of a humanized murine monoclonal anti-VEGF antibody that blocks all forms of VEGF-A (Eter et al. 2006). Initial trials compared ranibizumab intravitreal injections to verteporfin photodynamic therapy. The Minimally Classic/Occult Trial of Neovascular Age-Related Macular Degeneration (MARINA) and Anti-VEGF Antibody for the Treatment of Predominately Classic Neovascularization in Age-Related Macular Degeneration (ANCHOR) studies were two pivotal phase three trials that demonstrated the critical role of ranibizumab in patients with AMD. Both of these trials compared 0.3 mg and 0.5 mg intravitreal ranibizumab injection with either a placebo arm (MARINA) or with PDT treatment (ANCHOR). Approximately 40% of patients in both trials showed a three-line improvement in vision at month 24 (Hanout et al. 2013). Ninety-five percent of eyes treated with ranibizumab showed improvements in both studies (Eter et al. 2006). The side effects of ranibizumab include endophthalmitis (1%) and stroke (1.3%) (Eter et al. 2006; Hanout et al. 2013). Ranibizumab was thereafter approved by the FDA for the treatment of wet AMD in June 2006.

The HARBOR study is currently comparing the approved dose of ranibizumab (0.5 mg) with a higher dose (2.0 mg) for AMD.

Bevacizumab Bevacizumab is recombinant humanized murine monoclonal anti-VEGF antibody that was originally approved in humans for the treatment of metastatic colorectal cancer (Eter et al. 2006). Off-label treatments for CNV have been studied thoroughly. The SANA (Systemic Avastin for Neovascular AMD) study treated nine patients with bevacizumab infusion and found that after 12 weeks of treatment visual acuity improved by 12 letters and OCT showed decreased central retinal thickness (Eter et al. 2006). The bevacizumab for neovascular age-related macular degeneration (ABC) trial demonstrated visual acuity gain of more than 15 letters in 33% of patients treated with intravitreal injections of bevacizumab compared to only 3% of patients treated with PDT and in the placebo group (Hanout et al. 2013). Only 3% of patients experienced ocular inflammation after intravitreal bevacizumab injections. The CATT (Comparison of AMD Treatment Trial) and IVAN (Inhibit VEGF in Age-related choroidal Neovascularisation) studies both determined that

treatment outcomes with monthly intravitreal injections of bevacizumab were not statistically different from monthly treatments with ranibizumab (Hanout et al. 2013). Although the IVAN study found that bevacizumab and ranibizumab had similar safety profiles, the CATT study found that more systemic side effects were encountered in patients treated with bevacizumab versus ranibizumab (Hanout et al. 2013). To date, bevacizumab is not FDA approved for the treatment of CNV; however, many clinicians use intravitreal injections of bevacizumab off-label in the treatment of CNV due to its proven efficacy.

Aflibercept Aflibercept is a recombinant fusion protein made of the Fc portion of IgG1 (Immunoglobulin G1) and the extracellular domains of human VEGF receptors 1 and 2. It binds to both VEGF-A and VEGF-B with high affinity (Browning et al. 2012). The VIEW1 and VIEW2 phase three trials showed that aflibercept intravitreal injections were non-inferior and clinically equivalent to monthly ranibizumab injections (Hanout et al. 2013; Browning et al. 2012). Interestingly, one treatment method tested included three monthly loading doses and doses every other month thereafter. This treatment method was also shown to be as efficacious as monthly ranibizumab (Browning et al. 2012). As this treatment regimen requires fewer injections, owing to its longer proposed half-life, it may be beneficial to patients in terms of reducing treatment frequency and therefore any risks associated with the intravitreal injection. Aflibercept was approved by the FDA for the treatment of wet AMD in November of 2011.

Future

Anti-PDGF-β

The Ophthotech company has developed the pegylated aptamer E10030 which is an anti-PDGF-β agent. It is thought that adding an anti-PDGF-β agent to an anti-VEGF agent could improve the treatment of CNV by inhibiting the initiation, growth, maturation, and stabilization of the nascent blood vessels. A phase two study has recently demonstrated that a combination of ranibizumab and E10030 resulted in better visual improvement and visual acuity stabilization (Hanout et al. 2013). The combination therapy also increases the frequency of regression of CNV (Campochiaro 2013). The Ophthotech agent is thus a promising new agent that, when added to currently available treatments, may further improve visual acuity in patients suffering from CNV. Two phase three studies have therefore been recently initiated to further explore the potential of this new agent.

Prognosis

Untreated CNV has a poor prognosis with most patients progressing to complete loss of vision. With treatment, however, many patients are able to maintain or improve their visual acuity for improved quality of life. Response to treatment does vary from patient to patient and the best predictors of response are clinical. Patients with superior responses to treatment include those who present with earlier stage disease, at a younger age, with smaller CNV lesions and better baseline visual acuity (Finger et al. 2014). Poor prognoses even with treatment are associated with delayed treatment, subfoveal CNV, lower baseline visual acuity, lengthier duration of disease, and older age (Wang and Kang 2012). Interestingly, the effect of smoking on the prognosis of CNV is currently unknown (Finger et al. 2014). Three different studies showed different effects of smoking on CNV (good, bad, and inconclusive), and therefore more research is needed to determine the true effect.

Genetic factors may also affect anti-VEGF treatment response (Finger et al. 2014). Several studies suggest that patients with AMD who have known risk genes (complement factor H (CFH), AMS2/HTRA1) or VEGF polymorphisms tend to have poorer outcomes than AMD patients without the risk genes (Finger et al. 2014). Additional genetic studies are required to determine its role in predicting a patient's response to treatment and prognosis of CNV.

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Choroidal Neovascularization: Myopia

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Choroidal neovascularization (CNV) is a common cause of visual loss in pathologic myopia. Among patients aged less than 50, myopia accounted for 62% of cases of CNV (Cohen et al. 1996). CNV was initially described as Forster-Fuchs' spots corresponding to the fibrotic evolution of the CNV associated with a hyperpigmentation of the lesion. CNV was considered as one of the most severe complication of pathologic myopia. However, its prognosis was radically changed and improved by intravitreal injections of anti-VEGF agents.

Epidemiology, Risk Factors

CNV was reported to affect 5–12% of the eyes with pathologic myopia. Different studies, especially performed in Japanese patients, tried to recognize risk factors for the development of CNV in myopic eyes (Ohno-Matsui et al. 2003; Hayashi et al. 2005, 2010; Ikuno et al. 2010; Wakabayashi and Ikuno 2010). The only

recognized general factors are female gender, with two-thirds of patients being women, and older age. Presence of CNV in the fellow eye is also considered as a significant increase of risk. Local fundus risk factors are lacquer cracks and presence of patchy atrophy. The incidence of lacquer cracks in eyes with myopic CNV was found to be at least 75%. OCT and angiographies also helped to recognize choroidal filling delay and thin choroidal thickness as important risk factors. Both findings may explain the role of aging in the occurrence of myopic CNV. On the contrary, axial length or refractive error does not seem to constitute significant risk factors (Neelam et al. 2012).

Pathogenesis

While still discussed, pathogenesis of myopic CNV may involve an attempt of choroidal vessels to supply retinal oxygen to the outer retina, because choroidal thinning may result in outer retinal hypoxic changes with increase in VEGF production. Lacquer cracks may promote the extension of choroidal vessels into the sub-RPE space. Mechanical stretching may also enhance the choroidal thinning and production of VEGF. In summary, there are many anatomical and physiological changes attributable to myopia that could explain the occurrence of CNV in these eyes, but the exact role of each of these changes remains speculative (Spaide 2014).

Clinical Description

Symptoms of CNV in myopic eyes do not differ from those occurring in other conditions. Patients usually complain from visual loss, metamorphopsia, central scotoma, less frequently micropsia, or dyschromatopsia. The most typical myopic CNV present as small (<1 disk area) grayish subfoveal lesions. Subfoveal location of CNV was found in 58–70% of cases. Small hemorrhages are frequent. A dark border, corresponding to hyperpigmentation, may be observed, but usually in relatively ancient lesions. Large hemorrhages or lipid exudates are very uncommon (Soubrane and Coscas 2001).

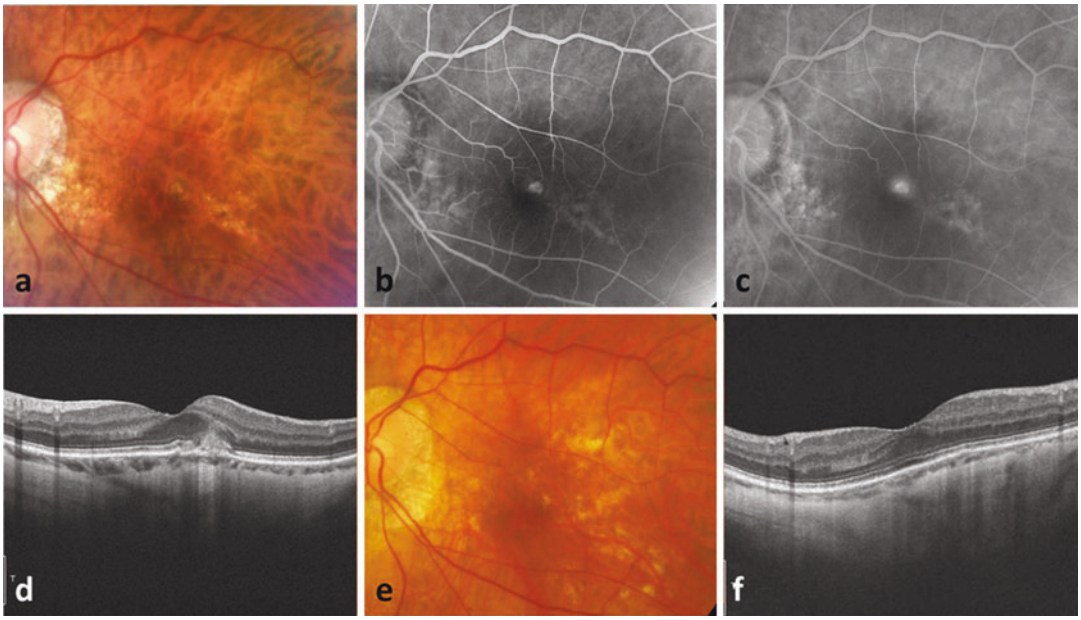
Fluorescein angiography demonstrates the CNV as "classic" or "type 2," characterized as an early hyperfluorescence associated with leakage of dye. This leakage may be minimal, especially in small lesions (Fig. 1). But, in other cases, it could be obvious. Indocyanine green angiography may be useful when the CNV is masked by hemorrhages and help to differentiate hemorrhages related to CNV from those that accompany the lacquer cracks formation. ICG angiography shows the CNV as a faint hyperfluorescent lesion. OCT usually shows the CNV as a localized thickening at the level of the subretinal space and the outer retina, giving a grayish appearance. This subretinal hyperreflective lesion may be accompanied by usually small amounts of intra- or subretinal fluid (Fig. 1).

Natural History

The natural history of myopic subfoveal CNV has been evaluated in various studies. Overall, less than one third of the eyes in the series reported retained visual acuity of more than 20/200, both in these studies and in the control group of one interventional prospective study (Chan et al. 2005; Soubrane 2008; Silva 2012).

Previous Therapeutic Options

Before the anti-VEGF era, treatment options were limited to laser photocoagulation for extra- and juxtafoveal CNV (Soubrane et al. 1986) and verteporfin (Visudyne, Novartis Pharma AG, Basel, Switzerland) photodynamic therapy (PDT) for subfoveal CNV (VIP-myopia). In the past, several alternative treatments were also advocated, including macular translocation (Mateo et al. 2004), surgical removal of CNV (Uemura and Thomas 2000), radiotherapy (Kobayashi and Kobayashi 2000), indocyanine green-mediated photothrombosis (Costa et al. 2003), transpupillary thermotherapy (Wu et al. 2008), and PDT combined with intravitreal triamcinolone (Chan et al. 2007a).



Choroidal Neovascularization: Myopia, Fig. 1 Subfoveal choroidal neovascularization. (**a**) Color photography: typical myopic fundus with tessellation and macular pigmentary changes. (**b**, **c**) Fluorescein angiography: early central hyperfluorescence with subtle leakage of dye in the late frame. (**d**) Horizontal scan of the OCT: *grayish* appearance of the outer retina, without significant thickening of the retina. (**e**, **f**) Color photograph and horizontal scan of the OCT after one intravitreal injection of ranibizumab: no scarring process of the retina, *restitutio ad integrum* of the foveal morphology

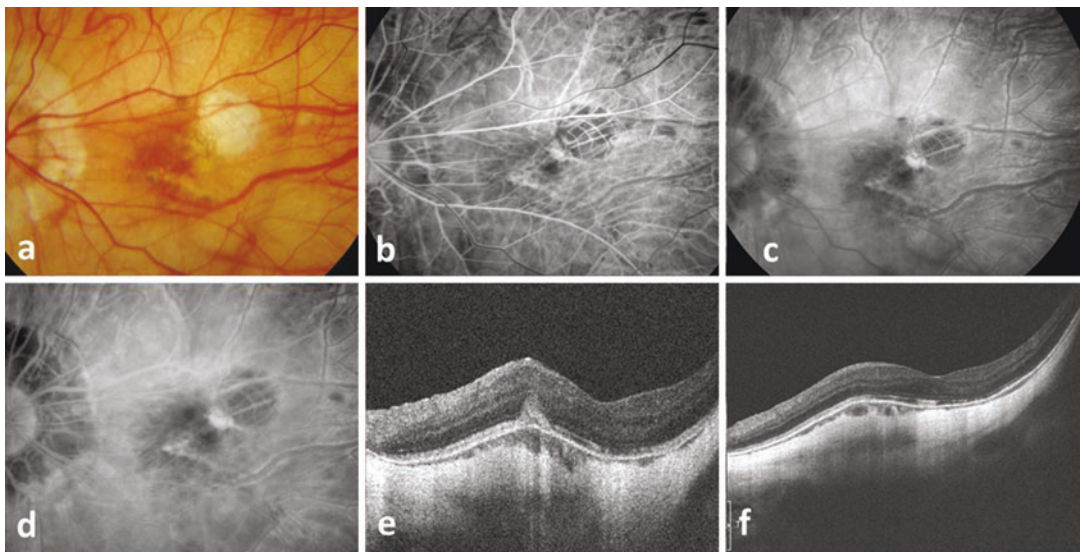
After laser photocoagulation, the first important step was the development of verteporfin therapy because it meant that patients with subfoveal CNV could now be treated. In most cases, the location of myopic CNV is indeed subfoveal. The results of a randomized, double-masked, placebo-controlled VIP study showed that at 1 year, visual loss of eight or more ETDRS chart letters occurred in 28% of treated eyes versus 56% of untreated eyes (Vip-Group 2001). However, at 2 years, the difference between these groups was no longer significant (Blinder et al. 2003). This limited long-term visual outcome was confirmed in subsequent studies (Schnurrbusch et al. 2005; Pece et al. 2006). In all these studies, final VA was found to be less than 0.3, in decimal equivalents, except for patients aged less than 55 (Lam et al. 2004) or treated only once (Chen et al. 2007). In clinical practice, verteporfin PDT was usually performed in subfoveal CNV because it was the only possible treatment. Its indications have been extended to juxtafoveal CNV and, even, to extrafoveal CNV.

Anti-VEGF Therapy

The development of anti-VEGF therapy over the past few years has revolutionized the management of exudative age-related macular degeneration, because for the first time, treatment with intravitreal ranibizumab (Lucentis, Genentech, Ca) proved effective in improving the mean VA of patients with subfoveal CNV. Bevacizumab, an inexpensive anti-VEGF agent whose structure is very close to that of ranibizumab, also became available and was widely used to treat this condition. As observed earlier for verteporfin PDT, the indication for intravitreal injections of anti-VEGF agents was rapidly extended to other diseases complicated by CNV. However, unlike what was done with verteporfin PDT, no manufacturer-sponsored randomized planned clinical trial of ranibizumab in myopic eyes was performed before 2012. So that use of anti-VEGF agents was discussed or controversial during many years (Rosenfeld 2007). However, data available

for pilot, monocentric, nonrandomized clinical studies all achieved similar results, including, in particular, significant improvement of VA (Laud et al. 2006; Chan et al. 2007b; Hernández-Rojas et al. 2007; Sakaguchi et al. 2007; Yamamoto et al. 2007; Arias et al. 2008; Rensch et al. 2008; Rhéaume and Sebag 2008; Silva et al. 2008; Dithmar et al. 2009; Gharbiya et al. 2009; Ikuno et al. 2009; Konstantinidis et al. 2009). In almost all series investigated, the gain in VA was important, usually more than three lines on ETDRS charts, after only a few injections. In all the series, safety was excellent, with no adverse events related to the drugs or to the procedure. Then, anti-VEGFs were rapidly considered as the first-line therapeutic option for management of myopic CNV (Cohen 2009). Recently, results of the RADIANCE study that compared verteporfin PDT with intravitreal ranibizumab have been recently reported (Wolf et al. 2014) and confirmed the excellent 1-year results obtained in another clinical study, named REPAIR (Tufail et al. 2013). The protocol of the RADIANCE trial has also compared two arms of patients treated with ranibizumab depending on their retreatment basis: one based on changes in VA and the other based on the disease activity. After 3 months, the eyes treated with ranibizumab gained 10.5 and 10.6 letters versus 2.2 letters, respectively, in the PDT arm. After 12 months, VA gains were of 13.8 and 14.4 letters, respectively, in the ranibizumab arms.

Anti-VEGF therapy is now the first-line treatment of myopic CNV. However, some questions remain. The first question concerns the choice of drug (ranibizumab, bevacizumab, or aflibercept). In AMD, clinical trials did not allow to observe differences in efficacy between ranibizumab and bevacizumab. The choice between the two drugs probably depends on the availability of anti-VEGF drugs, which may differ greatly from one country to another, on safety considerations and regulatory recommendations, and cost. There are no data in the literature concerning aflibercept. However, the results of the Phase 3 MYRROR study in myopic choroidal neovascularization (mCNV) have been reported in different meetings. In this trial, patients receiving aflibercept at an initial dose of 2 mg, followed by treatment on an as-needed (PRN) basis, had a mean



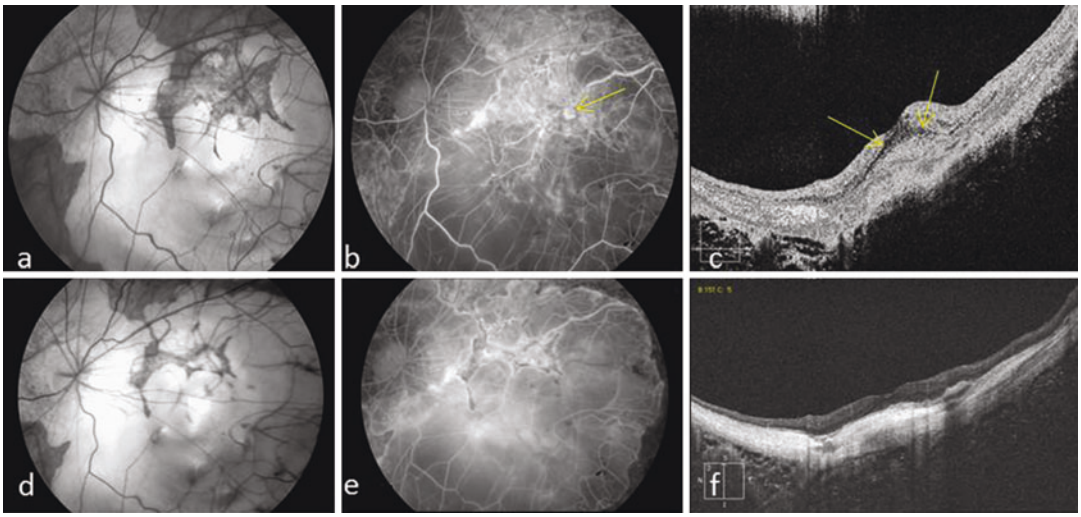
Choroidal Neovascularization: Myopia, Fig. 2 (**a**) Color photography: typical myopic fundus pallor, with an atrophic roundish lesion corresponding to a previous photocoagulation scar of a myopic CNV. (**b**–**d**) Fluorescein angiography: juxtafoveal recurrence of the CNV with moderate leakage of dye. (**e**) Horizontal scan of the OCT: *grayish* appearance of the outer retina, without significant thickening of the retina. (**e**, **f**) Color photograph and horizontal scan of the OCT after a single intravitreal injection of ranibizumab: restitution ad integrum of the foveal morphology

improvement in best-corrected visual acuity (BCVA) from baseline at week 24 of 12.1 letters, compared to a loss of 2.0 letters in patients receiving sham injections ($p < 0.0001$). There was no comparison with verteporfin or other anti-VEGF agents.

The second question is the protocol that should be used for treating myopic CNV with anti-VEGF drugs. The radiance trial results suggested the use of a PRN dosing after a single injection, with further treatment depending on the resulting VA and on fluorescein angiography and/or OCT findings. Indeed, one injection may be sufficient to allow the disappearance of the CNV (Figs. 1 and 2).

The third question is that of defining the follow-up protocol and the indications for reinjection during that period. An initial monthly follow-up is advised, but in absence of recurrence, the follow-up may be less strict than in AMD patients. Concerning detection of recurrences, the extent of the perfusion of the CNV may be difficult to evaluate without fluorescein angiography (FA). Furthermore, OCT is not easy to perform in myopic eyes and only gives a measurement of macular thickness, which is no more than an indirect index of leakage due to perfusion of the CNV. There is no formal recommendation for the follow-up of patients with myopic CNV treated with anti-VEGF agents. However, it could be advised to use all clinical parameters (visual loss, reoccurrence of metamorphopsia, appearance of hemorrhages) and perform OCT and/or fluorescein angiography in order to detect any sign of neovascular activity and decide re-treatments.

The last question is the long-term results of anti-VEGF in myopic CNV. In AMD, the long-term studies have shown a progressive decline of visual acuity with loss of the initial visual gain. Some studies addressed this question in myopic eyes with CNV. Extension of myopic atrophic changes may obviate the initial good visual results of anti-VEGF therapy (Fig. 3). Most of studies showed a small decline over time of the mean visual acuity of treated eyes attributable to occurrence of atrophic changes (or extension of pre-existing myopic atrophic changes) or, less frequently, to fibrosis or persistence of subretinal fluid. The decline was, however, relative. Indeed, all studies showed significant improvement



Choroidal Neovascularization: Myopia, Fig. 3 (**a**) Red-free photography: typical myopic atrophic changes. (**b**) Fluorescein angiography: subfoveal CNV (*arrow*). (**c**) Horizontal scan of the OCT: *grayish* appearance of the outer retina (*arrows*), with thickening of the retina. (**d**–**f**) Corresponding images 2 years after three intravitreal injections of ranibizumab: the CNV is no more present, but the initial gain in visual acuity was lost because of extension of the atrophic myopic changes

compared to baseline at 2, 3, or 4 years of follow-up (Franqueira et al. 2012; Lai et al. 2012; Peiretti et al. 2012; Oishi et al. 2013; Cohen et al. 2015). Thus, myopic CNV may be considered as a serious but usually treatable complication of pathologic myopia.

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C

Choroidal Osteoma

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Synonyms

Osseous choristoma

Definition

Benign choroidal tumor consisting of many osteocytes, osteoblasts, and a few osteoclasts that form interconnected bony trabeculae with large blood vessels.

Etiology

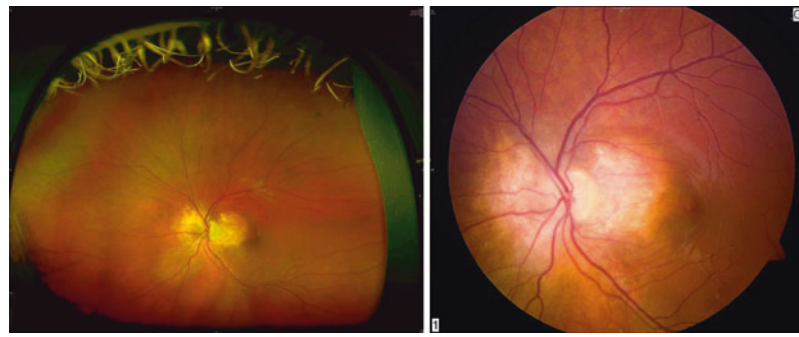
These tumors are usually choristomas in origin. There is some evidence to support both a genetic etiology, with some families having several members with the disease over several generations, and an inflammatory etiology following cases of choroiditis, posterior scleritis, and idiopathic orbital inflammation. The lesion is most common in women in their second to third decade and may be complicated by choroidal neovascularization (CNV) (Trimble and Schatz 1983; Horgan and Singh 2014).

Clinical Presentation

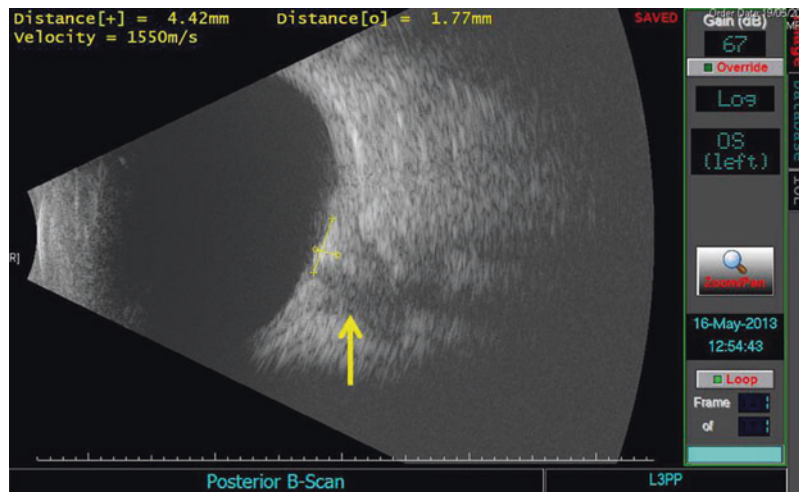
In most cases choroidal osteomas are unilateral, although bilateral cases have been reported. Choroidal osteomas appear as a flat yellow-white lesion with overlying retinal pigment epithelium (RPE) changes. The lesions are usually oval and have a clear irregular margin. The typical size is 1.5–2 disc diameters, although larger lesions have been reported. Lesions are usually located around the optic disc and may extend into the macula (Fig. 1). Calcifications are apparent on ultrasonography (Fig. 2). The osteomas usually grow slowly, but there have been rare reports of rapid growth on the one hand and of spontaneous regression on the other hand. The main complication, appearing in about half of the cases in the first decade after diagnosis, is choroidal neovascularization. Visual loss may result from the tumor itself, from neovascularization, or from damage to the optic nerve (Horgan and Singh 2014).

Diagnostics

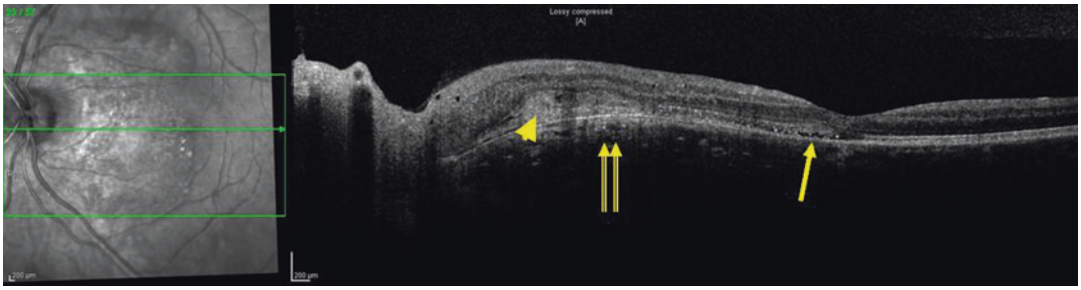
Clinical examination should be complimented by ultrasonography and fundus photography, along with optical coherence tomography (OCT) imaging to detect leakage from choroidal neovascularization (Fig. 3). B-scan ultrasonography is very sensitive in detecting the shadowing effect created by calcifications within the osteoma (Fig. 2). OCT can detect both subretinal and intraretinal fluids. If these fluids do not extend into the central macular area, they should not cause a visual disturbance and can remain untreated. There are typical angiographic signs of



Choroidal Osteoma, Fig. 1 Peripapillary and macular choroidal osteoma with an elevated *white-yellow* appearance (*left panel*, wide angle; *right panel*, 30° fundus picture)



Choroidal Osteoma, Fig. 2 B-scan ultrasonography demonstrates the shadowing effect (*arrow*) of the internal calcification



Choroidal Osteoma, Fig. 3 Optical coherence tomography (OCT) shows the sub-foveal fluid (*arrow*), the subretinal exudate (*arrowhead*), and the irregular shape of the choroid (*double arrow*) at the location of the osteoma

choroidal osteoma in both fluorescein angiography (FA) (early patchy hyperfluorescence and late staining) and in indocyanine green (ICG) angiography (early hypofluorescence and late diffuse staining). Angiography can also detect abnormal choroidal vessels with a lacy network with late leakage in FA. However, the clinical significance of finding non-leaking vessels is low, since standard treatments for CNV have limited success. Other forms of imaging, such as computed tomography (CT), can also detect the calcifications but are uncalled for when ultrasound is available.

Differential Diagnosis

Differential diagnosis includes ▶ malignant choroidal melanoma (amelanotic), ▶ choroidal hemangioma, choroidal metastasis from a distant primary malignancy, ▶ choroidal lymphoma, and ▶ posterior scleritis.

Clinically, the light-colored appearance of the osteoma may be seen in the lesions in the abovementioned list. The typical ultrasonic picture of internal calcification can also occur in a long-standing untreated choroidal hemangioma. However, posterior scleritis will also show a retrobulbar edema on ultrasound. Choroidal lymphoma has a similar clinical appearance and is usually a metastasis from systemic lymphoma with rare cases of primary choroidal lymphoma, which are hard to diagnose. It is the clinical combination of all the information that leads to the correct diagnosis, although follow-up may sometimes be the determining factor.

Prophylaxis

There are currently no methods to avoid development of a choroidal osteoma, or prevent the formation of CNV in this tumor.

Therapy

Replacement of normal choroidal vasculature by the osteoma cannot be reverted. Thus, the damage to the overlying RPE and retina is irreversible, and damaged areas will remain as a scotoma (blind spot). Similarly, if the osteoma grows around the optic nerve head and compresses it, treatment is of no avail. One can try and treat damage caused by leaking CNV. Sealing of the leaking vessels by laser photocoagulation has been replaced by PDT. Recent studies report on reducing the fluid via use of intravitreal injections of anti-vascular endothelial growth factor (anti-VEGF) (Bevacizumab, "Avastin") (Khan et al. 2014). However, the origin of the leaking vessels from an osteoma may render some protection, and only some of the patients benefit from any treatment in terms of improvement in visual acuity, whether there is any remaining sub- or intraretinal fluid or not. Therefore, stable amounts of sub- and/or intraretinal fluid that do not disturb vision can be left untreated.

Prognosis

As a benign tumor, choroidal osteoma does not threaten patients' lives, but after a decade most patients will lose vision down to 20/200 or less.

Epidemiology

This is a rare condition with an unknown incidence.

Cross-References

- ▶ Choroidal Hemangioma
- ▶ Lymphoma: Definition
- ▶ Malignant Melanoma (MM)
- ▶ Scleritis

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Choroidal Perfusion Abnormalities in the Preeclampsia, Eclampsia, and HELLP Syndrome Complex

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Definition

Pregnancy complicated with the abnormalities encompassed by the multisystemic spectrum of preeclampsia, eclampsia, or HELLP syndrome may be accompanied by segmental or generalized arteriolar spasm, arterial and venous occlusive disease, serous retinal detachments, and yellow, placoid discolorations of the retinal pigment epithelium. These manifestations are due to vascular compromise in the retinal and choroidal circulations and are predominantly transient.

Preeclampsia is an obstetrical complication that typically develops after the 20th week of pregnancy and is characterized by hypertension, proteinuria, and generalized edema. It is subclassified as mild and severe and upgraded to eclampsia when it is superimposed by seizures. The Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy released in November 2013 recommended that the presence of alternative systemic findings observed with new-onset hypertension can fulfill the diagnosis of preeclampsia even in the absence of proteinuria, defining as one of the alternative systemic findings the "cerebral or visual symptoms." The HELLP syndrome, on the other hand, consists of hemolysis, elevated liver enzymes, and low platelets and is generally associated with severe preeclampsia or eclampsia.

Etiology

Preeclampsia is a syndromic condition that affects all organ systems, with repercussions that go far beyond hypertension and renal dysfunction and with placental dysfunction at its genesis. The latter is generally understood as an immunologically altered function of trophoblasts, which impairs vascular remodeling of the maternal spiral arteries that perfuse the placenta, with resultant placental hypoperfusion and increased blood velocity. This derangement of placental perfusion is believed to, in turn, cause a multisystemic maternal disease via a series of mediators, which include modifiers of angiogenesis and vascular endothelial function. The fetus is endangered due to placental vascular insufficiency. It is common knowledge that preexisting chronic hypertension in an expecting mother can manifest as severely increased blood pressure and this chronic hypertension, defined as

"hypertension that predates pregnancy," can be associated with fetal morbidity, expressed as intrauterine growth restriction. One of the main challenges in the care of pregnant women with chronic hypertension is to be able to distinguish whether chronic hypertension has worsened or preeclampsia has settled in, as the maternal and fetal morbidity are significantly augmented in case preeclampsia superimposes.

The choroidal perfusion abnormalities precipitated by preeclampsia's cascade of events range from a focal necrosis of the choriocapillaris to a fibrinoid necrosis of the larger caliber arterioles. The preeclampsia-induced choroidopathy is upheld to be ischemic in nature based on the features observed on clinical examination (small choroidal infarcts, ultimately manifesting as foci of atrophy and pigmentary hyperplasia, namely, the Elschnig spots), as well as the fluorescein and indocyanine green angiography findings. Areas of choroidal non-filling in angiograms can be differentiated from patchy choroidal filling, by an absence of choroidal fluorescence that persists for over 5 s and correspond to the serous retinal detachment areas. In the context of severe, generalized vasospasms that occur in preeclampsia, it has been noted that the posterior ciliary artery blood flow velocity is also increased in this disease, suggesting a vasospasm. Despite the rich circulation of the choroid, its vessels lack autoregulative defenses to hypertensive spikes. Also, a rapid deceleration of the arteriolar flow occurs in the choroid, as the blood flows in a terminal fashion from a functional perspective, given that its arterioles run a short course and undergo minimal branching. This enables damage to occur when acute, severe attacks of hypertensive spasms are swiftly transmitted downstream, causing focal choroidal edema and ischemia. After a focal occlusion occurs in the choroid, there is negligible collateral flow. Furthermore, preeclampsia may be associated with a perfusion dysfunction that goes beyond mere hypertensive spasms, as vascular endothelial function may be altered by a variety of putative mediators, activating intravascular coagulation with consecutive microcirculatory blockage. The microemboli are more likely to lodge at the choroidal capillaries given the large volumetric arteriolar flow that decelerates rapidly.

The putative mechanism of the development of serous retinal detachments and yellow, opaque areas of discoloration in the retinal pigment epithelium is that the ischemia at the choriocapillaris level may lead to retinal pigment epithelium ischemia, which causes malfunction of its fluid pump, leading to the accumulation of the subretinal fluid associated with ischemic damage at the retinal pigment epithelium level, manifested as deep, yellow lesions.

Clinical Presentation

The preeclamptic syndrome has been associated with a spectrum of posterior segment findings that include a retinopathy similar to hypertensive retinopathy, consisting of severe, segmental, or generalized arteriolar spasms, arterial occlusions, and venous occlusive disease. However, serous retinal detachments and yellow, placoid discolorations of the retinal pigment epithelium are features not commonly encountered in hypertensive retinopathy. Retinal manifestations may be more common in expecting mothers with preexisting hypertension. Acutely severe hypertension is associated with spasm of the central retinal artery, as suggested by the increased central retinal artery blood flow velocity. Saito et al. have suggested that while retinopathy is more frequently seen in preeclampsia superimposed on preexisting hypertension, the presence of serous retinal detachments and yellow deep retinal pigment epithelium discolorations are more specific to preeclampsia and eclampsia.

Symptomatically, preeclamptic patients may present with blurry vision, scotomata, and photopsia. However, choroidal perfusion abnormalities may be observed funduscopically in the absence of significant retinal vascular abnormalities and are associated with yellow, placoid areas of retinal pigment epithelium change. The neurosensory detachments are typically bilateral and bullous.

Diagnostics

Fluorescein angiography (FA) and indocyanine green angiography (ICG) are helpful in assessing the perfusion abnormalities seen in eclampsia. Aside from visualizing the degree of retinal nonperfusion, areas of choroidal nonperfusion in the FA can be differentiated from patchy choroidal filling by an absence of choroidal fluorescence that persists for over 5 s and correspond to the serous retinal detachment areas. In the context of severe, generalized vasospasms that occur in preeclampsia, it has been noted that the posterior ciliary artery blood flow velocity is also increased in this disease, suggesting a vasospasm. ICG demonstrates areas of ischemia accompanied by staining and hyperpermeability of the choroidal vessels.

Differential Diagnosis

The incidence of central serous chorioretinopathy (CSC) may be increased in pregnancy and shares characteristics with the choroidopathy in eclampsia. Both can have bullous elevation of the retina; however, central serous chorioretinopathy tends to be unilateral. FA in CSC shows a focal RPE leak and possibly the classic smokestack pattern of dye accumulation in the subretinal space. Choroidal vascular dilatation, leakage, and staining may be seen on ICG. Neither FA nor ICG will show ischemia in CSC.

Prophylaxis

Prenatal care includes monitoring for, and early treatment of, preeclampsia. Close follow-up is of paramount importance for women who have had a previous pregnancy complicated by preeclampsia. There is no specific ophthalmic prophylaxis.

Treatment

Early detection and treatment of preeclampsia and careful management of eclampsia and HELLP syndrome are crucial in preventing the development or treating the manifested ocular complications of this syndrome complex, since no specific ophthalmic treatment exists for them.

Prognosis

All serous retinal detachments and retinal pigment epithelium discolorations observed in a series of 40 eyes studied by Saito et al. came to a resolution with the delivery, except for three eyes with a large, geographic pattern of retinal pigment epithelium lesions that went on to develop significant chorioretinal atrophy.

Epidemiology

Preeclampsia affects an estimated 3–7% of all pregnancies. Risk factors include nulliparity, extremes of mother's age, African-American ancestry, multi-fetal gestations, preexistence of hypertension, or renal pathology. Serous retinal detachment secondary to choroidal hypoperfusion is a relatively rare yet well-reported cause of vision loss in this multisystemic perfusion and metabolic derangement. In the previously mentioned study by Saito et al., 65% of the eyes (40 out of 62 eyes of 31 patients with preeclampsia or eclampsia) was found to have serous retinal detachments, and 58% (36 of 62 eyes) had retinal pigment epithelium lesions that were located in the peripapillary or macular regions.

The choroidopathy manifested as serous retinal detachments does not appear to be an additional risk factor in potential adverse neonatal outcomes. The detachments generally resolve with complete restoration of visual acuity within a few weeks. However, there are a few reports of persisting changes for over a year after pregnancy or chronic changes that were later in life thought to represent tapetoretinal degenerations.

Chromatic Aberration: Definition

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Synonyms

Axial chromatic aberration; Lateral chromatic aberration; Longitudinal chromatic aberration; Transverse chromatic aberration

Definition

Due to the dispersion of refractive materials (i.e., glass, water, ocular media, etc.), the focusing properties of a lens depend on the wavelength of light. Chromatic aberration is generally manifested in two ways: focusing error and magnification error. Dispersion-induced focusing error is known as *axial* or *longitudinal chromatic aberration* and is illustrated in Fig. 1. The axial chromatic aberration of the eye over the visible spectrum is approximately 2 diopters (Thibos et al. 1992), as shown in Fig. 2. Due to the positive Abbe number of the ocular media, shorter wavelengths (blue colors) are relatively hyperopic to the longer wavelengths (red colors).

Dispersion-induced error in magnification is known as *transverse* or *lateral chromatic aberration*. Both types of chromatic aberration increase as the pupil size increases; however, only transverse chromatic aberration increases with retinal eccentricity.

Cross-References

▶ Dispersion: Definition

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Chronic Actinic Keratopathy

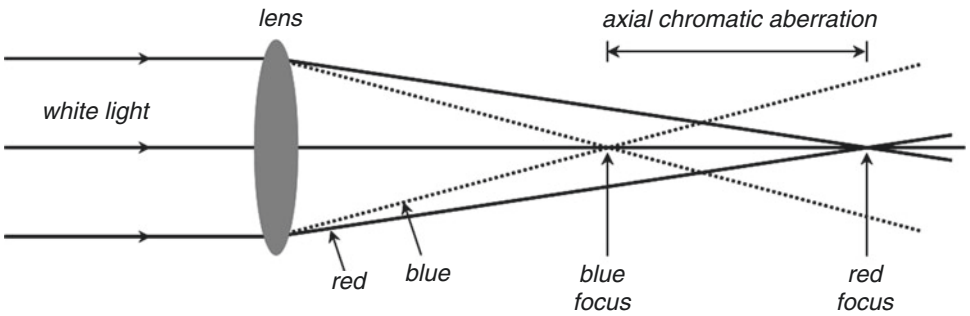
▶ Keratinoid (Spheroidal) Degeneration
▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
▶ Spheroidal Degeneration

Chronic Conjunctivitis

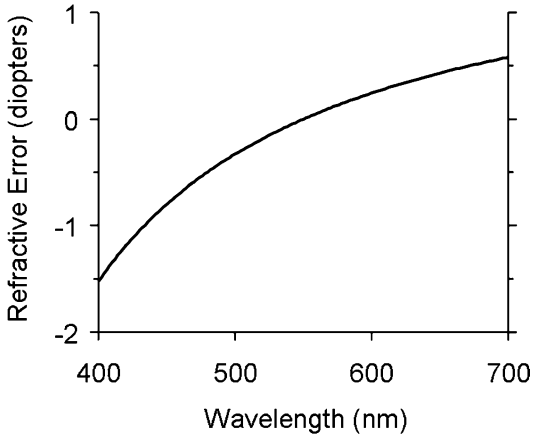
▶ Canaliculitis

Chronic Follicular Conjunctivitis

▶ Chlamydia



Chromatic Aberration: Definition, Fig. 1 Axial chromatic aberration



Chromatic Aberration: Definition, Fig. 2 Refractive error as a function of wavelength in the human eye. Data from data published by Thibos et al. (1992)

Chronic Progressive External Ophthalmoplegia Plus Disease

► Kearns Syndrome

Chronic Serpiginous Ulcer of the Cornea

► Mooren Ulcer

Chrysiasis, Corneal Pigmentation

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Synonyms

Ocular chrysiasis

Definition

Chrysiasis is the deposition of gold in bodily tissues after the long-term administration of gold therapy, most commonly in the treatment of rheumatoid arthritis.

Etiology

Chrysiasis generally results from medical treatment of disorders such as rheumatoid arthritis with injection or oral therapy with gold.

Clinical Presentation

Gold deposits are visually asymptomatic, but may be seen in both the cornea and the conjunctiva. In the cornea, the deposits are at the level of the posterior stroma and Descemet's membrane. They consist of yellow-brown granules which may have a metallic sheen. Gold deposits may very rarely also appear in the lens.

Diagnosis

Chrysiasis would be diagnosed with careful examination of the cornea and conjunctiva under slit-lamp exam.

Differential Diagnosis

Other causes of pigmented deposits of the posterior stroma include copper deposits or a mottled cyan opacification associated with long-term soft contact lens wear. The cause of this opacification is unclear. Copper deposition has been associated with most commonly Wilson's disease. Non-pigmented deposits can be caused by cornea farinata, pre-Descemet's corneal dystrophy, X-linked ichthyosis, and ocular argyrosis. Crystalline dystrophies or keratopathies may also be confused with this disease process.

Prophylaxis

Preventing ingestion of gold would prevent this process from occurring.

Therapy

As chrysiasis is visually asymptomatic, there is no therapy for this entity.

Prognosis

Prognosis is good as chrysiasis will remain visually asymptomatic requiring no treatment. In some cases, the depositions may clear after the cessation of therapy, while in others the depositions never disappear.

Epidemiology

Chrysiasis is found in individuals undergoing medical treatment of disorders such as rheumatoid arthritis who may get gold injections or gold oral therapy. Almost all patients who have received greater than 1,500 mg of gold therapy develop gold deposits.

Cross-References

- ▶ Bietti Crystalline Retinopathy
- ▶ Schnyder Crystalline Dystrophy Syndrome

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Ciliary Arteries

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Definition

Branches of the ophthalmic artery, these arteries or their subsequent branches supply the anterior optic nerve, choroid, choriocapillaris, rectus muscles, iris, and ciliary body.

Basic Characteristics

Variable numbers and branches of the ciliary arteries have been reported. Typically, however, a medial and lateral posterior ciliary artery arise from the ophthalmic artery and penetrate the globe a few millimeters to either side of the optic nerve. Each of these divides into one long posterior ciliary artery and 7–10 short posterior ciliary arteries. The former course along the horizontal meridians, branch at the ora serrata, and help supply the anterior choriocapillaris and ciliary muscle; the latter supply the posterior choriocapillaris, peripapillary choroid, and anterior optic nerve.

Cilioretinal arteries arising from the ciliary arteries are present in 20–25% of eyes; by perfusing certain portions of the macula, they may afford preservation of vision after central artery occlusion.

The muscular branches of the ophthalmic artery supply the rectus muscles and form the anterior ciliary arteries. Each rectus muscle has two arteries except the lateral rectus, which only has one. Further anteriorly, the anterior ciliary arteries penetrate the sclera posterior to the limbus and supply the iris (major arterial circle), ciliary body, and anterior choroid. Branches which do not penetrate the sclera, but continue toward the limbus, merge with subconjunctival vessels to form the episcleral plexus.

Anterior segment ischemia may occur following extraocular muscle surgery. The horizontal muscles have collateral circulation between the long posterior ciliary arteries and the anterior ciliary arteries; however, the vertical muscles do not. Therefore, anterior segment ischemia usually is seen only when multiple muscles and at least one vertical rectus muscle have been involved.

Cross-References

- ▶ Ciliary Body
- ▶ Ophthalmic Nerve
- ▶ Optic Nerve Head
- ▶ Pigment Epithelium, Ciliary Body, and Iris

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Ciliary Block (Malignant) Glaucoma, Muscarinic Antagonists for

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Synonyms

Aqueous misdirection; Direct lens block angle closure; Malignant glaucoma

Definition

In ciliary block glaucoma, there is an accumulation of aqueous humor in or behind the vitreous (rather than flowing normally from the posterior chamber into the anterior chamber), causing a forward shift of the vitreous and forward movement of the lens-iris diaphragm resulting in a shallow anterior chamber.

Etiology

The mechanism of ciliary block glaucoma is not clearly understood. The ciliary body may form a seal around the lens or anterior hyaloid preventing the anterior flow of aqueous. The anterior hyaloid may contribute to this blockage by pushing forward against the ciliary body as fluid collects posteriorly. As intraocular pressure increases, flow of fluid through the vitreous decreases, contributing further to the vicious cycle of elevated intraocular pressure and collection of fluid in the vitreous. Lastly, laxity of lens zonules allowing anterior movement of the lens may also contribute. Ciliary block glaucoma occurs after intraocular surgery, especially after glaucoma surgery on patients with angle-closure glaucoma.

Clinical Presentation

On exam, the anterior chamber is shallow peripherally and centrally. Intraocular pressure is normal to elevated. Clear pockets of fluid may be seen within the vitreous. On ultrasound biomicroscopy, ciliary processes can be seen rotated anteriorly.

Diagnostics (Lab Diagnostics)

It is important to rule out suprachoroidal hemorrhage by exam or echograpy and rule out pupillary block glaucoma by creating an iridotomy.

Differential Diagnosis

1. Pupillary block glaucoma. Often associated with peripheral iris bombe and deeper central anterior chamber; can be eliminated by iridectomy or iridotomy

2. Choroidal detachment. Usually associated with low intraocular pressure
3. Suprachoroidal hemorrhage. Often associated with pain and elevated intraocular pressure

Prophylaxis

Cycloplegic therapy at the time of glaucoma surgery may be helpful.

Therapy: The two main components of therapy are cycloplegia and intraocular pressure management. Atropine can be used daily to four times per day and may act to tighten the zonules to break ciliary block. Intraocular pressure can be controlled with hyperosmotics such as oral glycerol or intravenous mannitol, as well as topical agents including carbonic anhydrase inhibitors, -blockers, and α_2-agonists, or oral agents including methazolamide or acetazolamide.

If medical management is not effective, surgery is considered. If the individual is aphakic or pseudophakic, the Nd:YAG laser can be used to rupture the anterior hyaloid face(thereby allowing trapped fluid behind hyaloid face to come forward) or the argon laser can be used to shrink ciliary processes if they are visible through an iridectomy (this can break the seal between the ciliary body and lens). If these attempts fail, pars plana tap of the vitreous or pars plana vitrectomy with removal of the anterior hyaloid may be needed.

Prognosis

Fifty percent of individuals are effectively treated within 5 days with medical therapy alone. Sometimes long-term use of cycloplegic-mydriatic therapy is necessary.

Epidemiology

Occurs in 0.6–4% of incisional surgeries for angle-closure glaucoma.

Cross-References

▶ Conjunctival Hemorrhage
▶ Pupillary Block

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Ciliary Block "Malignant" Glaucoma

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Synonyms

Aqueous misdirection syndrome

Definition

The term malignant glaucoma was coined by von Graefe in 1869. He noted that following peripheral iridectomy for acute angle-closure glaucoma, a number of patients developed shallowing of the anterior chamber together with high intraocular pressure. The subsequent prognostic outlook for such eyes was typically poor, hence the term "malignant."

Classically, malignant glaucoma is characterized by a shallow anterior chamber associated with raised intraocular pressure and in the presence of a patent iridotomy (Ruben et al. 1997).

Etiology

Malignant glaucoma occurs in 2–4% of eyes undergoing surgery for angle-closure glaucoma and may occur at any time following surgery, from the first postoperative day to many years later. Usually it occurs after filtering surgery in eyes with angle closure but has also been described after surgical iridectomy and after cataract surgery. There are also reports of the condition after laser iridotomy, Nd-YAG laser cyclophotocoagulation, or holmium laser sclerostomy.

The exact mechanism of malignant glaucoma remains unclear. Shaffer proposed misdirection of aqueous either into or around the vitreous, but recently Quigley questioned that mechanism and proposed that malignant glaucoma involves a vicious cycle in the behavior of the vitreous gel, but without a one-way valve or aqueous misdirection (Quigley 2009). Acute choroidal expansion induced by the sudden surgical decompression of the eye causes immediately postoperative IOP elevation and leads to increased aqueous outflow and development of a substantial posterior-anterior pressure gradient. This differential leads water to move from the posterior vitreous cavity toward the posterior chamber. Since most adult eyes have a posterior vitreous detachment to some degree, fluid from behind the vitreous must pass through the gel to equalize this pressure difference. Normal vitreous does, however, limit the free passage of water, and its fluid conductivity decreases under an increased pressure differential. In persons with extremely poor vitreous conductivity, this leads to a vicious cycle. The vitreous is unable to equalize the pressure difference, and it compresses. The vitreous and the iris and lens move together toward the cornea as aqueous leaves the trabecular meshwork (or the fistula).

Clinical Presentation

Following filtration surgery malignant glaucoma presents as a shallow anterior chamber with a normal or high intraocular pressure in the presence of a patent peripheral iridectomy. There is axial shallowing of the anterior chamber, and, unlike pupil block, the iris is not typically bowed forward.

Diagnostics

The configuration of the anterior segment structures shows iridocorneal touch and appositional angle closure in the presence of a patent iridotomy or iridectomy. A pooling of aqueous between the posterior capsule and the anterior hyaloid face may be visible especially in the cases of pseudophakic malignant glaucoma. Using high-resolution ultrasound, anterior rotation of the ciliary body with apposition to the iris should be detectable.

Differential Diagnosis

Angle closure caused by pupil block may be distinguished by the typical bowing of the iris. If the patency of the iridotomy is in doubt, a repeat laser iridotomy should be performed (Rauscher and Parrish 2008). A shallow anterior chamber associated with a wound leak should be easily detectable and will usually be associated with hypotony. If the iridotomy is patent and the intraocular pressure high, choroidal hemorrhage must be excluded either clinically or by ultrasound examination. In the absence of a history of surgery, other causes of secondary angle closure including intumescent lens, choroidal neoplasm, central retinal vein occlusion, and secondary pupil block must be excluded.

Prophylaxis

Filtering surgery in eyes with angle-closure glaucoma should only be performed when all other therapeutic modalities have failed to adequately lower IOP. Treating angle-closure glaucoma (after

iridotomy) with cyclophotocoagulation may not only lower IOP but also be preventive for malignant glaucoma by shrinking ciliary processes. If filtering surgery has become mandatory, a two-stage procedure with previous cataract extraction by phacoemulsification or one-stage combined procedures (phacotrab) should be preferred. Tight closure of the flap and a large-sized iridectomy should be performed. Leaving some viscoelastics in the anterior chamber at the end of surgery may be of some use to prevent anterior chamber shallowing. In small eyes prone to pseudophakic malignant glaucoma, the size of IOL optics should not exceed 6 mm.

Therapy

Management of ciliary block glaucoma is in the first instance medical. This consists of cycloplegic drops, topical beta-blockers, apraclonidine, oral carbonic anhydrase inhibitors, and, if necessary, oral glycerol or intravenous mannitol. This combination reduces choroidal expansion, shrinks the vitreous, decreases aqueous production, and encourages backward displacement of the lens-iris diaphragm. Fifty percent of cases will be relieved within 5 days. If high pressure continues after this time, or if lens-corneal touch occurs, surgical intervention should be considered. Once the anterior chamber deepens and the IOP has been normalized, medical treatment can be gradually withdrawn. The patient may be maintained on atropine alone, but may require indefinite treatment with atropine to prevent recurrence.

Direct argon laser treatment through a peripheral iridectomy to shrink the ciliary processes may be used. In aphakic or pseudophakic eyes, Nd-YAG laser may be used to perform posterior capsulotomy/hyaloidotomy. Recently, diode laser cyclophotocoagulation has been shown to be very effective in treating malignant glaucoma (Bresson Dumont et al. 2006).

If none of the above is enough to maintain anterior chamber depth and to lower IOP, surgery must be considered. In phakic eyes, phacoemulsification and in the bag IOL is the first step or is performed as combined procedure with vitrectomy (Sharma et al. 2006). Usually a vitreous tap has to be performed first to adequately lower the IOP and enable safe phacoemulsification. When phacoemulsification is finished, a core vitrectomy is performed either via an anterior approach using a posterior capsulorhexis or a pars plana approach. Excision of posterior capsule and partial zonulectomy must be included in the procedure creating a direct communication between vitreous cavity and the anterior chamber through an iridectomy.

Prognosis

Approximately 50% of cases will be permanently under control with medical treatment alone. Long-term treatment with atropine carries however a substantial risk of allergic reactions. Surgical treatment has a high success rate of up to 90% if combined procedures (i.e., phacoemulsification and vitrectomy) are used in cases of pseudophakic malignant glaucoma. In the majority of cases, however, the IOP-lowering success of the filtering surgery is lost, and the patient may require further glaucoma treatment.

Epidemiology

Malignant glaucoma occurs in 2–4% of eyes undergoing surgery for angle-closure glaucoma. Pseudophakic malignant glaucoma is rare (less than 0.1%).

Cross-References

▶ Angle-Closure Glaucoma
▶ Nanophthalmos

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Ciliary Body

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Definition

A structure containing muscle, vessels, epithelium, and autonomic neural tissue that is attached at the scleral spur and is composed of the pars plicata (with its ciliary processes) and pars plana, that has several functions, including creating the supraciliary space adjacent to the sclera, producing aqueous humor, maintaining a portion of the blood-aqueous barrier, and allowing accommodation and uveoscleral outflow. It is considered to be part of the uveal tract (along with the choroid and iris).

Cross-References

► Accommodation, Cataract
► Pars Plana; Pars Plicata

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Ciliary Ganglion

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Definition

The ciliary ganglion (CG) is a parasympathetic ganglion responsible for miosis (pupil constriction) in response to light and accommodation. Parasympathetic, sympathetic, and sensory fibers run through the CG but only the parasympathetic fibers synapse in the CG. It is located in the posterior orbit.

Anatomy

The parasympathetic fibers originate from the parasympathetic brainstem nuclei then travel with the oculomotor nerve (cranial nerve III) which then enters the posterior orbit through the superior orbital fissure. After synapsing in the CG, the parasympathetic fibers continue to the eye via the short ciliary nerves. These postganglionic fibers control miosis by innervating sphincter pupillae, and they

control accommodation by innervating the ciliary body muscle. Disruption of the parasympathetic fibers can result in anisocoria.

In contrast, postganglionic sympathetic fibers, which originate from superior cervical ganglia, branch off of the carotid plexus surrounding the internal carotid artery, pass through the superior orbital fissure, and then continue through the CG on the way to the eye. Upon exiting the CG, these sympathetic fibers travel with parasympathetic fibers in the short ciliary nerves. These sympathetic fibers are responsible for mydriasis (pupil dilation) in response to dark ambient lighting conditions by innervating the dilator muscle.

General sensory fibers, the ophthalmic branch of the trigeminal nerve (cranial nerve V_1), also enter the orbit through the superior orbital fissure. V_1 provides innervation for general ocular, orbital, and periorbital sensation, including nasociliary, frontal, and lacrimal branches. Some fibers from V_1 pass through the CG and travel along the short ciliary nerves to the eye. These fibers provide sensation to the cornea and can be tested with the corneal reflex. Other fibers from V_1 travel along the nasociliary nerve and become a part of the long ciliary nerves.

Clinical

Disruption of the parasympathetic fibers to the eye can result in anisocoria that is greater in the light. Disruption of sympathetic innervation to the eye can result in an ipsilateral Horner syndrome, characterized by ptosis, miosis, and anisocoria in the dark, and anhidrosis, but typically damage to the CG results in parasympathetic dysfunction-related anisocoria worse in the light. Most cases of CG damage are idiopathic (e.g., Adie tonic pupil), but some occur after orbital infection, surgery, or trauma to the CG. Disruption of V_1 fibers to the eye can result in loss of sensation to the cornea and will result in a negative corneal flex test. Depending on the location of the lesion along these nerves, facial sensation can be lost as well.

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Ciliary Muscle

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Definition

The ciliary muscle is a ring muscle located within the ciliary body which controls by its contraction and relaxation the tension of the zonular fibers and thereby the shape of the crystalline lens with accommodation.

Anatomy

The ciliary muscle is a smooth muscle with some peculiarities in its structure and function (fast contraction and relaxation, tendons at the origin and point of insertion, parallel orientation of myofibrils). Its cross-sectional shape is triangular. It consists of three groups of muscular fibers differing in situation and orientation within the ciliary body. These groups are the longitudinal, radial, and equatorial or circular fibers. It is found in the outer part of the ciliary body where its fibers originate from a ring-shaped tendon which is fixated at the scleral spur. Neighboring structures are the sclera and the collagen fibers, fibroblasts, and melanocytes of the outer face of the ciliary body. The inner surface of the ciliary muscle borders anteriorly to the pars plicata and posteriorly to the pars plana of the ciliary body. The anterior insertion is at the scleral spur and the trabecular meshwork. Posteriorly it is fixated to the stroma of the choroid by elastic tendons.

Neural and Blood Supply

The mesodermal smooth muscle is supplied by the short ciliary nerves carrying postganglionic parasympathetic fibers from the ciliary ganglion. Preganglionic fibers originate in the Edinger-Westphal nucleus in the midbrain and run to the ciliary ganglion in the inferior portion of the third cranial nerve. There is also a weak reciprocal sympathetic innervation of the ciliary muscle inserting the orbit from the carotid plexus together with the first branch of the fifth cranial nerve where they join the long and short ciliary nerves. The blood supply of the ciliary muscle comes from the anterior and posterior ciliary arteries. Venous drainage is posteriorly to the vortex veins.

Function

Contraction of the ciliary muscle pulls the suspension of the lens which causes relaxation of the zonular fibers. As a consequence, the crystalline lens is molded into a more convex shape by its elastic capsule and the eye is focused to a nearer distance (Glasser et al. 2003).

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Ciliary Spasm

► Accommodation, Functional (Nonorganic/Nonphysiologic) Disorders of

Circle of Zinn-Haller

► Annulus of Zinn

Circular Polarization

► Circularly Polarized Light

Circularly Polarized Light

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Synonyms

Circular polarization

Definition

A special case of polarized light where the electric field vector does not alter its amplitude but its orientation of oscillation. If the light wave is observed at a given time t, the electric field vector describes a helix along the direction of the beam. Circular polarization of light is used in ophthalmology to control reflection glare in fundus photography. Scanning laser polarimetry is based on that principle.

Cross-References

► Circular Polarization

CLAL

► Transplantation

Classic Lattice Corneal Dystrophy, LCD Type 1 and Biber-Haab-Dimmer

► Stromal Dystrophies

Classic LCD

▶ Lattice Dystrophy

CLAU

▶ Transplantation

Claude Syndrome

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Definition

Claude syndrome refers to the set of signs and symptoms associated with unilateral tegmental lesions of the dorsomedial midbrain. Named after Henri Charles Jules Claude, who described the condition in 1912, this particular intramedullary brainstem syndrome most commonly involves unilateral infarction of the medial half of the red nucleus and superior cerebellar peduncles after decussation.

Etiology

Infarction of the dorsomedial midbrain may arise secondary to occlusion of a branch of the posterior cerebral artery. These events are most commonly caused by preexisting cerebrovascular disease or malignancy. Large artery disease producing emboli or in situ thrombosis account for the majority of mesencephalic infarct mechanisms, while cardioembolism and small-vessel disease are associated with 25% of cases.

Disruption of blood flow in the posterior cerebral artery may compromise the following neuronal tracts within the midbrain tegmentum, thus yielding the characteristic signs and symptoms of this stroke syndrome: red nucleus, superior cerebellar peduncles after decussation, dentatorubro fibers, oculomotor nerve nucleus, and fibers. Insult to fourth nerve fascicles, the medial lemniscus and the medial longitudinal fasciculus have been observed.

Clinical Presentation

Patients with *Claude syndrome* present with ipsilateral oculomotor nerve palsy and contralateral cerebellar hemiataxia and tremor. The third nerve palsy is usually a partial palsy characterized by ptosis, a dilated pupil, and downward (hypotropia) and lateral deviation (exotropia) of the involved eye. Features of cerebellar hemiataxia involve asynergy of upper and lower limbs, poor gait, and dysdiadochokinesia. Cerebellar tremor may be referred to as a rubral tremor or intention tremor and presents with dysmetria or the lack of coordination of a limb to move accurately to an intended position.

Patients may also have a dissociated horizontal nystagmus of the abducting eye due to internuclear ophthalmoplegia when medial longitudinal fasciculus axons are injured. Further, due to the proximity of fourth nerve fibers to the posterior cerebral artery in the midbrain, patients may concurrently present with a fourth nerve palsy.

Diagnostics

Appropriate neuroimaging (i.e., magnetic resonance imaging, computed tomography) should

be directed to the dorsomedial midbrain in patients presenting with *Claude syndrome*.

Differential Diagnosis

Differential diagnoses for *Claude syndrome* generally include other intramedullary brainstem syndromes (e.g., Benedikt, Wallenberg, Weber, Nothnagel, Parinaud, von Monakow, Millard-Gubler, Avellis, and Jackson syndromes).

Prophylaxis

Evaluation and management of underlying risk factors for cerebrovascular disease should be considered.

Therapy

Treatment is directed toward the underlying etiology.

Prognosis

Prognosis for *Claude syndrome* is variable and dependent upon the severity and extent of the underlying disease process affecting the dorsal midbrain.

Epidemiology

Ischemic cerebrovascular disease increases with age, but other underlying risk factors for ischemia can occur in younger patients, in either gender and in any ethnic group.

Cross-References

- ▶ Cerebrovascular Accident (CVA)
- ▶ Fourth Nerve Palsy
- ▶ Red Eye
- ▶ Third Nerve Palsy

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Clear Cell Hidradenoma

▶ Hidradenoma, Clear Cell (Eccrine Acrospiroma)

Clear Cell Myoepithelioma

▶ Hidradenoma, Clear Cell (Eccrine Acrospiroma)

Clear Corneal Incision

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Synonyms

Tunneling

Definition

A surgical technique of small-incision cataract surgery. The incision affects only the cornea and therefore does not depend on a conjunctival dissection. There are three forms of clear corneal incisions: uniplanar, biplanar, and triplanar.

The advantages are an easier access of the phacoemulsification tip and the self-sealing occlusion of the incision, so that sutures are not necessary. The incision is favorable to foldable intraocular lens implants and frequently used after or with fistulation operations from the temporal. Furthermore, this technique reduces the possibility of bleeding and allows a local noninvasive anesthesia. Anticoagulants should not be discontinued.

History

The idea dates back to 1992 when Fine first described a new concept of a planar temporal clear corneal sutureless and self-sealing incision (single-plane clear corneal incision). The position of incision was chosen by picking the point with the largest distance to the corneal center on the temporal median. Fine affirmed this incision was easier, quicker to realize, and astigmatically neutral. Other authors modified the description. Kellar favored a "sclera-less" clear corneal incision beneath a short conjunctival flap. Williamson and Langerman introduced hinged clear corneal incisions (shallow-groove two-plane incision and deep-groove two-plane incision). Ernest ascertained that corneal healing proceeded faster when the fibroblastic healing response was allowed to start at the conjunctival limbus (7 days compared with 1 month with other techniques). Neuhann and Ernest described in 1996 the posterior limbal incision as equal in aesthetics and surgical efficiency, slightly superior in patient comfort, and far more stable.

Clinical Features

Tunneling is conducted by using a diamond keratome (corneatome), 90° tip, 45°shoulders, and double-beveled edges. The line of intersection should be drawn obliquely, immediately anteriorly to the limbal vascular arcade. During this process, a limbal fixation ring may stabilize the eyeball. The slit knife cuts at a depth of 1, 5–2 mm; its tip is turned posteriorly to perforate Descemet's membrane. The resulting incision is 3 mm and thus sufficient for emulsification and implantation of foldable intraocular lenses. A biplanar incision may be performed by modifying the angle of penetration.

Tests

In advance to prepare for the clear corneal incision, an efficient examination of the eyes and the acquisition of the patient's anamnesis with possible past eye surgeries are elementary to determine any exclusion criteria.

Differential Diagnosis

Other cataract wound incision techniques:

- Sclera tunnel incision (traditional curvilinear, straight and frown incisions)
- Posterior limbal incision

Etiology

See "History" section above.

Treatment

See sections "Differential Diagnosis" and "Clinical Features" above.

Cross-References

- ▶ Cataract Surgery
- ▶ Limbal Relaxing Incisions
- ▶ Microkeratome
- ▶ Scleral Tunnel

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Clear Lens Exchange (CLE)

▶ Refractive Lens Exchange

Clear Lens Extraction

▶ Refractive Lens Exchange

Climatic Droplet Keratopathy

▶ Keratinoid (Spheroidal) Degeneration
▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
▶ Spheroidal Degeneration

Climatic Droplet Keratopathy (Spheroidal Degeneration)

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Synonyms

Many different names have been applied to the different manifestations of what may be a single pathological response in the cornea (Gray et al. 1992). These names were based on race, geography, occupation, clinical appearance, presumed etiology, presumed nature of the corneal deposits, and eponyms, including:

- The blindness of Dahalach
- Tropical corneal dystrophy
- Nodular band-shaped dystrophy of tropical countries of arid soil
- Fisherman's keratopathy
- Labrador keratopathy
- Nama keratopathy
- Eskimo keratopathy
- Bietti's nodular corneal dystrophy
- Degeneratio corneae sphaerularis elaioides
- Degeneratio primaria oleoguttata centrale et superficiale
- Band-shaped nodular dystrophy
- Nodular band-shaped hyaline keratopathy
- Spheroidal degeneration
- Spheroidal keratopathy
- Gelatinous dystrophy
- Droplet keratopathy
- Droplet degeneration of the cornea
- Colloid degeneration of the cornea
- Hyaline corneal degeneration
- Keratinoid corneal degeneration
- Keratoid corneal degeneration
- Proteinaceous corneal degeneration
- Elastotic degeneration of cornea
- Elastoid degeneration
- Corneal elastosis
- Chronic actinic keratopathy
- Band-shaped climatological degeneration

Chronic actinic keratopathy describes a condition associated with conjunctival elastosis and typified by characteristic extracellular concretions (Klintworth 1972). A later publication found this entity and others, including Labrador keratopathy, to fit the classification of the clinical term "spheroidal degeneration" (Fraunfelder and Hanna 1973). Several other reported clinical entities describe globular deposits of the cornea that may represent the same condition, with geographic variations or subtypes:

- Spheroidal keratopathy
- Spheroid degeneration
- Hyaline corneal degeneration
- Colloid degeneration of the cornea
- Sphaerularis elaiodes
- Superficial central primary degeneration oleogutta
- Degeneratio hyaloidea grannuliformis corneae
- Bietti corneal degeneration
- Nodular corneal dystrophy in tropical arid countries
- Nodular hyaline, band-shaped keratopathy
- The blindness of Dahalach
- Fisherman's keratopathy
- Band-shaped nodular dystrophy of the cornea
- Labrador keratopathy
- Keratoid corneal degeneration
- Climatic droplet keratopathy
- Chronic actinic keratopathy
- Proteinaceous corneal degeneration
- Elastoid degeneration
- Elastotic degeneration
- Eskimo corneal degeneration

Definition

A degeneration of the cornea and/or conjunctiva characterized by the appearance of fine, golden yellow, spherules or globules of varying size at or beneath the epithelium. A degeneration characterized by the appearance of yellow or golden globules of varying size in the superficial cornea or conjunctiva.

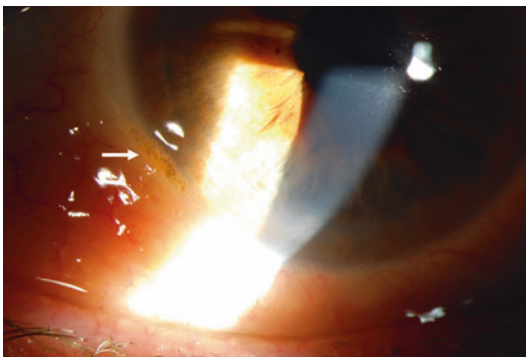
Etiology

The exact source of the protein material forming the droplets is unknown. It has been postulated that the material may result from the actions of ultraviolet light on serum proteins that diffuse into the cornea from limbal vessels (Farjo and Sugar 2009). Increasing age and exposure to ultraviolet light are the most common associated factors. Other proposed risk factors include dry eyes, malnutrition, corneal trauma or microtrauma (wind, sand, ice), low humidity, and extremes of temperature. Associated ocular diseases include keratitis, lattice corneal dystrophy, and glaucoma (Fraunfelder and Hanna 1973).

Clinical Presentation

The clinical appearance is characterized by the presence of yellow or golden spherules or "droplets" at or beneath the corneal or conjunctival epithelium (Fig. 1). The spherules, or globules, are generally clear but may become more opaque over time and range in size from approximately 0.1–0.6 mm in diameter. These lesions are located in the superficial corneal stroma, Bowman's membrane, subepithelium, and occasionally in the epithelium in advanced degeneration (Magovern et al. 2004).

The clinical presentation has been classified as primary corneal, secondary corneal, and conjunctival forms (Gray et al. 1992). In the primary form, the lesions are typically seen at the horizontal limbus within the palpebral fissure, and there is no evidence of other corneal pathology. With progression, the spherules enlarge and spread toward the central cornea. In the secondary corneal form, the lesions are less likely to assume a band-shaped configuration and may be concentrated around areas of prior scarring, neovascularization, or inflammation. The lesions are generally bilateral except in secondary cases where there is associated unilateral pathology such as scars, trauma, or



Climatic Droplet Keratopathy (Spheroidal Degeneration), Fig. 1 Multiple golden spherules are visible along the limbus (white arrow)

keratitis. In the conjunctival form, lesions occur interpalpebrally at the 3 and 9 o'clock positions and are frequently found in association with pinguecula.

A modified grading system has been used to describe the distribution and visual effects of the globular deposits (Johnson and Ghosh 1975).

Trace: Deposits seen in very small numbers. One eye only affected or only one end of interpalpebral strip in each eye if bilateral.

Grade 1: Involvement of medial and lateral interpalpebral strips, with sparing of central cornea.

Grade 2: Central cornea affected, but not enough to affect visual acuity.

Grade 3: Central cornea affected, and vision reduced.

Grade 4: Elevated nodules present in addition to findings of Grade 3.

Diagnosis

Diagnosis is made clinically based on the characteristic appearance. Biopsy with histologic examination can support or confirm the diagnosis but is not typically required. Histologically, deposits appear as extracellular amorphous globules, which may coalesce to form larger masses in Bowman's membrane (Farjo and Sugar 2009).

Differential Diagnosis

Similar appearing clinical entities include corneal amyloid degeneration, gelatinous drop-like corneal dystrophy (familial subepithelial amyloidosis), band keratopathy, climatic proteoglycan stromal keratopathy, primary lipoidal degeneration of the cornea, Salzmann nodular degeneration, and limbal girdle of Vogt (type II).

Prophylaxis

Unknown. Based on the recognized association with sunlight exposure, it is plausible that methods to reduce sunlight exposure could potentially reduce the development or progression of climatic droplet keratopathy.

Therapy

Treatment is rarely required since the majority of individuals are asymptomatic. In patients with loss of vision from central corneal lesions, treatment can be considered. Possible treatment options include superficial keratectomy, phototherapeutic keratectomy, lamellar keratoplasty, or penetrating keratoplasty depending on the depth and density of the lesions.

Prognosis

The majority of individuals do not develop any symptoms and progression is slow in the primary form. However, progression may result in loss of vision, particularly in areas of the world where climatic exposure is severe. Visual acuity may be affected due to involvement of the visual axis of the cornea or from irregular astigmatism. In advanced disease, accumulation of globular masses or plaques may cause heaping up of the corneal surface, epithelial defects, and recurrent corneal erosions. Corneal sensation may be reduced, and sterile ulceration may rapidly progress to microbial keratitis or perforation (Ormerod et al. 1994).

Epidemiology

The prevalence varies based on geographic location with rates of 6% in England and over 60% in males in Labrador (Farjo and Sugar 2009). It is approximately three times more common in males and increases with age, being found in roughly 50% of patients over 70 years of age (Fraunfelder and Hanna 1973). It is most frequently seen in areas with high sunlight exposure. While the primary form is generally considered a degeneration, there are rare reported cases describing a more dystrophic form that may be familial and occurs in relatively young patients without a history of other ocular disease or environmental exposure.

Cross-References

- ▶ Keratinoid (Spheroidal) Degeneration
- ▶ Keratopathy Actinic (Labrador Keratopathy/ Spheroidal Degeneration)
- ▶ Spheroidal Degeneration

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Clinically Definite MS

- ▶ Poser Criteria, for Multiple Sclerosis

Clinically Significant Macular Edema (CSME)

- ▶ Diabetic Macular Edema

Closed Angle

- ▶ Angle Closure

CMV Retinitis

- ▶ Cytomegaloviruses, Retinitis

CN III Palsy

- ▶ Third Nerve Palsy

C

CN IV

- ▶ Cranial Nerve IV (Trochlear Nerve), CNIV

CN VII Palsy

- ▶ Bell's Palsy

CNIII

- ▶ Cranial Nerve III (Oculomotor Nerve)

CNVI

- ▶ Cranial Nerve VI (Abducens Nerve)

CO_2 Laser

- ▶ Carbon Dioxide Laser

Coats' White Ring

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Synonyms

Corneal white dot

Definition

Coats' white ring is a superficial ring of iron deposition that occurs after a metallic foreign body is removed.

Etiology

It appears as a tiny ring of white dots, most often inferiorly. It is thought to result from previous iron deposition by a corneal foreign body and occurs long after resolution of the corneal iron ring. It has no symptoms and it represents an incidental finding. The ring may be oval and incomplete, and small white opacities may be seen inside. Epithelium remains intact, and it has been localized just deep to the corneal epithelium in the anterior portion of Bowman's membrane.

Classification

1. Trauma.
2. Occupational: when working with limestone, there may be deposition of some of the substance's components, especially calcium oxide, in the cornea.

Cross-References

- ▶ Corneal Degenerations
- ▶ Corneal Pigmentations
- ▶ Iron, Corneal Deposits of
- ▶ Rust Ring, Iron Foreign Body Causing

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Cogan Microcystic Dystrophy

▶ Corneal Dystrophies

Cogan Microcystic Epithelial Dystrophy

▶ Map-Dot-Fingerprint Dystrophy (Epithelial/Anterior Membrane Dystrophy)

Cogan Syndrome

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Synonyms

Nonsyphilitic interstitial keratitis

Definition

Rare multisystem disease that affects the cornea by causing stromal interstitial keratitis and the vestibuloauditory system by causing vertigo and deafness.

Etiology

An autoimmune disorder but the exact etiology is unknown, possible immune reaction to a common autoantigen in the cornea and middle ear (Kanski and Bowling 2011). The disease also shares some clinicopathologic features with polyarteritis nodosa (Skuta et al. 2011–2012).

Clinical Presentation

Usually affect young adults. The majority of the patients report an upper respiratory tract infection few weeks before the onset of ocular or vestibuloauditory symptoms (Snow and Wackym 2009). The most common eye finding is a chronic bilateral interstitial keratitis; it begins with faint paralimbal (peripheral) subepithelial infiltrate of the cornea, and the patient may complain of irritation, photophobia, redness, and decreased vision. Later those lesions may progress centrally associated with deep stromal vascularization that may eventually regress leaving ghost vessels. Rarely, anterior uveitis, episcleritis, scleritis, and retinal vasculitis may develop, and these signs represent atypical Cogan syndrome (Yanoff and Duker 2004). The vestibuloauditory symptoms include tinnitus and vertigo followed by progressive sensorineural hearing loss mostly bilateral but can start in one ear and quickly (within days) progress to the other ear. Other systems (heart, gastrointestinal, renal, respiratory) may be involved as well. Small percentage of patients (10%) may develop severe vasculitis similar to polyarteritis nodosa (Yanoff and Duker 2004).

Diagnosis

Mainly clinical and after other causes of interstitial keratitis especially syphilis (by obtaining VDRL/FTA-ABS) has ruled out. Audiologic test could be helpful to look for typical sensorineural hearing loss.

Differential Diagnosis

It includes other causes of keratitis with vestibuloauditory symptoms:

- Syphilis (congenital or acquired)
- Sarcoidosis
- Polyarteritis nodosa
- Wegener's granulomatosis
- Vogt-Koyanagi-Harada disease
- Sympathetic ophthalmia

Prophylaxis

Unclear.

Therapy

It is important to have high index of suspicion for this disease as it usually leads to permanent hearing loss within months if not treated. Treatment consists of high-dose oral corticosteroid with the possibility of adding immunomodulatory therapy if response to corticosteroid was not sufficient. Keratitis is treated with topical corticosteroids. A multidisciplinary approach that involves an ophthalmologist, otolaryngologist, and an internist is advised.

Prognosis

With adequate treatment and early recognition, the prognosis of ocular and auditory symptoms is usually good.

Epidemiology

Affect young adults (peak incidence in third decade of life) with both sexes affected equally, and it is more common in Caucasians (Snow and Wackym 2009).

Cross-References

- ▶ Sarcoidosis
- ▶ Syphilis: Overview
- ▶ Wegener Granulomatosis

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Cogan Type

► Congenital Ocular Motor Apraxia

Cogan's Apraxia

► Congenital Ocular Motor Apraxia

Cogan-Reese Syndrome

► Iridocorneo Endothelial Syndrome

Collamer Intraocular Lens

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Synonyms

ICL; Implantable collamer lens; Implantable contact lens; Posterior chamber phakic intraocular lens

Definition

A phakic IOL that is placed between the iris and the crystalline lens fixated in the ciliary sulcus (Kohnen and Koch 2006).

Epidemiology

Today, the number of implanted ICL is higher than implanted PRL, but lower than the lastest anterior chamber angle (AcrySof) and iris-supported phakic IOL models (Artisan/Verisyse and Artiflex/Veriflex).

History

Complications from anterior chamber angle-supported implants led to the idea of moving toward the posterior chamber. This location theoretically provided lower incidence of halos and glare as the margins of the pupil cover the border of the optical zones. Additionally, the risk of corneal endothelial damage was also theoretically minimized, due to the greater distance between the implant and the corneal endothelium. One of the first posterior chamber phakic IOL designs, the "collar-button" or "mushroom" configuration, is attributed to Fyodorov in 1986 (Fechner and Alpor 1986). He developed a one-piece silicone lens, with a 3.2-mm optic and a concave anterior surface that projected anteriorly through the pupil. The lens was fixated behind the iris plane by two haptics and had a total length of 8.0 mm. Initial complications included corneal touch, decentration, pupillary block glaucoma, iridocyclitis, and cataract formation. Since then, evolution in design and materials has led to the emergence of several different models, including the Adatomed lens. However, cortical opacities and decentration frequently occurred after surgery, and this lens was also withdrawn from the market. Currently, there are only two posterior chamber models available on the market: the "Implantable Contact Lens" (ICL, STAAR Surgical, Monrovia, USA) and the "Phakic Refractive Lens" (PRL, Carl Zeiss Meditec, Jena, Germany) (Hardten et al. 2003).

Clinical Features

This lens is made of collamer which is a mixture of 0.2% collagen and 60% HEMA copolymer. This material attracts deposition of a monolayer

of fibronectin on the lens surface that inhibits aqueous protein binding and makes the lens invisible to the immune system. ICL's design and materials were refined through a series of prototypes in different clinical trials. For models V (Version) 2 and 3, complications reported were small percentages of pupillary block and pigment dispersion glaucoma. However, late anterior subcapsular opacities of the crystalline lens occurred and were attributed to intermittent contact between the ICL and the crystalline lens. The current model, Visian ICL V4, is a rectangular single-piece lens, 7.5–8 mm wide, available in four overall lengths: 11.5–13.0 mm in 0.5-mm steps for myopic and 11.0–12.5 mm in 0.5-mm steps for hyperopic lenses. Optic diameter ranges from 4.65 to 5.5 mm in myopic IOL, depending on the dioptric power. In hyperopic ICLs, optic diameter is always 5.5 mm. Available powers for myopic lenses range from −0.5 to −18.0 D, for hyperopic lenses from +0.5 to +10.0 D, and for toric ICLs correcting myopia with added positive cylinder of +1.0 to +6.0 D. ICL thickness is less than 50 μm at the optic zone, 500–600 μm at the haptic zone, and 100 μm at the haptic footplates.

Tests

Anterior chamber depth for ICL implantation must be at least 2.8 mm for myopic and at least 3 mm for hyperopic lenses. Other inclusion criteria for phakic IOL implantation must be considered (see also "▶ Phakic Intraocular Lens").

Differential Diagnosis

The other posterior chamber phakic IOL is the PRL that floats freely between the iris and the crystalline lens.

Etiology

Other currently available types of phakic IOLs are anterior chamber angle (AcrySof) or iris-supported phakic IOLs (Artisan/Verisyse and Artiflex/Veriflex) (Güell et al. 2010).

Treatment

Correct loading of the ICL in the cartridge and the injector is essential for easy implantation. The ICL has two tiny holes on the footplates (distal right and proximal left) that allow anterior-posterior orientation of the lens. The cartridge is filled with viscoelastic substance. The lens is loaded with dome up, taking special care of a correct haptic position avoiding their rupturing. A piece of soft material, the Staar Foam-tip, is positioned to protect the ICL from contact with the plunger of the shooter. Broad mydriasis is essential for uneventful implantation. The ICL may be inserted through a sub-3 mm incision. One or two side-port incisions of about 1 mm and 90° separated from the main incision are created. The anterior chamber is filled with viscoelastic. The cartridge is inserted bevel-down, and ICL is carefully injected. It is essential to control unfolding of the lens, so as to twist the bevel right or left to assure a correct orientation of the lens. Finally, the haptics are gently pushed under the iris with a blunt spatula. As correct centration of the ICL and position of the haptics in the ciliary sulcus is checked, acetylcholine is injected in the anterior chamber to induce pupil constriction. In hyperopes a peripheral iridectomy should be performed to prevent pupillary block situation. Alternatively, one or two Nd:YAG laser iridotomies are performed in the peripheral iris one week preoperatively. In myopes, the lastest Version of the ICL implements a central hole (aquaport) in the optic of the lens so that an iridectomy/iridotomy is not necessary any more.

Cross-References

- ▶ Foldable Intraocular Lens
- ▶ Intraocular Lens
- ▶ Phakic Intraocular Lens
- ▶ PRL Phakic Intraocular Lens
- ▶ Verisyse Iris-Supported Phakic Intraocular Lens

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Collier Tucked Lid Sign

► Collier's Sign

Collier's Sign

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Synonyms

Collier tucked lid sign; Posterior fossa stare

Definition

Retraction of the upper eyelids in primary gaze or upgaze, resulting in a "staring" expression, can be due to the Collier lid retraction sign. Unlike the typical lid retraction seen with thyroid eye disease, downgaze is usually normal and usually no lid lag occurs (Lee and Brazis 2011), but patients with the full dorsal midbrain syndrome may have ophthalmoplegia (e.g., bilateral upgaze palsy) that might mimic thyroid eye disease.

Etiology

The etiology varies based on the patient's age group, but is usually due to damage to the pretectal area or dorsal midbrain (Parinaud syndrome). The lid retraction is thought to be due to disinhibition of the central caudal nucleus and excess activation of the levator palpebrae superioris muscle, which raises the eyelid. There is often an associated bilateral upgaze palsy, and lid retraction can worsen with attempted upgaze (Campbell 2013), but other features of the dorsal midbrain syndrome may also be present (e.g., convergence-retraction nystagmus and light near dissociation of the pupils). Any lesion in the dorsal midbrain may produce the Collier sign including infectious, inflammatory, vascular, neoplastic, demyelinating, traumatic, toxic, and shunt malfunction or hydrocephalus.

Occurrence

Although there is no gender or racial predilection for the Collier sign, age at onset may be helpful in the differential diagnosis. In children, neoplastic (e.g., pinealoma), congenital (e.g., aqueductal stenosis, hydrocephalus), or infectious etiologies (e.g., postviral) predominate. In contrast in adults, demyelinating (e.g., multiple sclerosis), traumatic, neoplastic (e.g., dysgerminoma), or vascular etiologies (e.g., arteriovenous malformation) are more common. In the elderly, ischemic (e.g., midbrain stroke), neoplastic, or, less likely,

vascular (e.g., posterior fossa aneurysm) can result in the Collier sign (Kanski 2010).

The Collier lid retraction sign may or may not be associated with other features of the dorsal midbrain syndrome (e.g., upgaze palsy, light near dissociation of the pupils, convergence-retraction nystagmus).

Classification

Signs and symptoms

Cross-References

- ▶ Arteriovenous Malformations (AVMs)
- ▶ Parinaud (Dorsal Midbrain) Syndrome
- ▶ Progressive Supranuclear Palsy
- ▶ Vertical Gaze Palsy

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Colloid Degeneration of the Cornea

- ▶ Keratinoid (Spheroidal) Degeneration
- ▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
- ▶ Spheroidal Degeneration

Color "Blindness"

- ▶ Anomalous Trichromats

Color Blindness

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Synonyms

Color vision deficiency; Dyschromatopsia

Definition

Color blindness is an inaccurate term that is used by many in reference to a wide range of deficiencies in color vision. Color vision disorders range from a very mild deviation from normalcy that can be identified only under laboratory condition to a very severe condition expressed as complete loss of ability to separate between different colors. Therefore, it is preferable to define disturbances in color vision as color vision deficiency or disorders in color visions, terms that cover the entire spectrum of color vision defects.

Etiology

Color vision disorders can be inherited or acquired, and it can arise from different pathological mechanisms, some are specific to color vision, and others are more general. Normal color vision depends upon undisturbed transmission of colored visual images from the outside world to the retina. The retina contains rod photoreceptors and three populations of cone photoreceptors, each containing a visual pigment of unique absorbance spectrum. Rod photoreceptors do not participate in color vision except under mesopic conditions. Under photopic conditions, light-induced electrical activities in the three populations of cone photoreceptors interact in post-receptoral neurons of the retina and are

transmitted to the brain as color-coded electrical signals. These color-coded messages reach specific regions in the brain, where further processing occurs, leading eventually to color perception.

Primary inherited color vision deficiency is present from birth and is similar in the two eyes, reflecting a mutation in one, two, or even three genes coding the protein part of the cone visual pigments. In one specific case, primary inherited complete color blindness arises from a mutation not associated with the genes coding the cones' visual pigments, but with the genes coding proteins specific for the cone phototransduction process, including transducin, PDE, or the cGMP-dependent cationic channels in the cone's outer segment.

Secondary color vision deficiency starts after birth and results from diseases of the visual system that can be inherited or acquired. Any abnormality in the ocular media, the functional integrity of the cone photoreceptors, the neural connections within the retinal cone systems, or color information processing in the brain can lead to disturbances in color vision. (i) Selective absorbance of certain wavelengths by the ocular media due to cornea opacity, cataract, or vitreous hemorrhage can lead to color vision disorder. This type of color vision defect worsens as the underlying cause develops, but disappears when the underlying cause is treated by corneal transplant, cataract extraction, or vitrectomy, respectively. (ii) Any disorder in the integrity of the cone photoreceptors, like cone dystrophy or cone-rod dystrophy, is expected to cause non-specific color vision disorders that worsen with time as the cone dystrophy progresses. (iii) In retinitis pigmentosa, a cone-rod dystrophic disease that affects primarily rod photoreceptors, a transient color vision disorder along the blue-yellow axis (tritanopia-like), can develop; the patient behaves as if the functional integrity of the short-wavelength cone photoreceptors is reduced compared to the function of medium- and long-wavelength cone photoreceptors. (iv) Patients with inherited or acquired disorders of the central retina, the macula, such as central serous retinopathy or Stargardt's disease suffer from color vision deficiency as well, starting usually as tritanopia-like defect, but can develop with time to a more general, unspecified color vision disorder. However, in these cases the color vision defect is limited to objects illuminating the macula. The color of large objects illuminating large retinal regions can be perceived correctly because peripheral cone photoreceptors are not damaged. (v) Glaucoma is a very common ocular condition associated with optic nerve damage and dropout of ganglion cells. In review of patients with open-angle glaucoma, only 20–40% of patients had normal color discrimination, 30–50% had tritanopia-like defects, and 5% showed red-green defects (Pacheo-Cutillas et al. 1999). (vi) Optic neuritis, an inflammatory disease of the optic nerve, causes reduction in visual acuity and specific effect on the perception of colors. Patients usually report on desaturation of colors, especially of red colors. (vii) A lesion along the visual cortical pathways may result in different degrees of acquired color vision deficiency, even to complete loss of color vision (achromatopsia). Notably, some reports describe patients suffering from cerebral achromatopsia, but normal visual acuity and normal visual fields (Hart 1987; Celesia and Brigell 2005).

Occurrence

Primary inherited color vision deficiency is one of the most common inherited visual disorders, with prevalence of up to 8% in males and 0.5% in females (Simunovic 2010). This gender-wise difference in prevalence is explained by the localization of two out of three cone opsin genes (the long and medium wavelengths) on the X-chromosome.

Anomalous red/green trichromacy and red/green dichromacy constitute the majority of cases of primary inherited color vision deficiency. Other forms, tritanomaly and tritanopia, are very rare and affect males and females alike at an occurrence of about 1 out of 500. Rod monochromacy (achromatopsia) or cone monochromacy (incomplete achromatopsia), which is usually accompanied with visual defects beyond color discrimination, is much more rare. Rod monochromacy occurs in 1 out of 50,000, and blue-cone monochromacy occurs in 1 out of

100,000, while green-cone or red-cone monochromacy occurs in 1 out of 1,000,000 or may be even 1 out of 100,000,000.

The prevalence of secondary color deficiency depends on the prevalence of the primary disorder itself. In contrast to primary inherited color vision deficiency, the prevalence is similar among males and females.

Classification

Color vision deficiency can be divided into two major classes: primary inherited color vision deficiency and secondary color vision deficiency.

1. *Primary inherited color vision deficiency* (Simunovic 2010): In a normal observer, there are three types of cone photoreceptors, each containing a different visual pigment with a different absorption spectrum – long-wavelength, medium-wavelength, and short-wavelength visual pigments. Therefore, a normal observer is characterized by trichromatic color vision.

   Three major types of primary color vision deficiency exist:

   (i) Anomalous trichromat: Subjects possess three classes of cone photoreceptors, but the visual pigment in one cone population is of abnormal structure, and therefore, its absorption spectrum differs slightly from that of the normal.

   (ii) Dichromat: One of the three cone visual pigments is missing or is not functional, and the remaining two cone visual pigments are normal. Therefore, color vision depends upon two populations of cones with different visual pigments instead of three, as in individual with normal trichromatic color vision.

   (iii) Monochromat: These can come in two forms – cone monochromat and rod monochromat. Cone monochromats in which only one spectral type of cone population is present are usually blue-cone monochromat, but cases of red-cone monochromat and green-cone monochromat have also been reported. Since, under mesopic condition, rods and cones can interact to give some degree of color vision, cone monochromats are also referred to as incomplete achromats. Rod monochromats, also known as achromats, possess no functioning cones; correspondingly, they suffer also from photophobia and reduced visual acuity.

2. *Secondary color vision deficiency*: The type of secondary color vision defect is not easy to classify, and its severity can progress with age as the underlying disease progresses. However, if the underlying defect is treated, the resulting color vision defect may disappear or at least weakens in severity. Diseases of the visual system causing color vision defects may affect any level of the visual system from the optical system to the brain. Köllner's rule, stating that patients with retinal disease develop blue-yellow discrimination loss, while optic nerve disease causes red-green discrimination loss, was historically used to classify acquired deficiencies. Exceptions to this rule include glaucoma, a disease of the ganglion cells and nerve fiber layer, which is primarily associated with blue-yellow defects, and also some retinal disorders such as central cone degeneration, which may start with blue-yellow defect but progresses to red-green defects and eventually to a general defect in color vision. Currently, the most widely used classification of secondary color vision disorders is Verriest's classification, which largely divides acquired color disorders into three types (Pinckers 1982):

   Type I – protanopia-like, with mild to severe confusion of red-green hues, little or no loss of blue-yellow color discrimination, and severe reduction visual acuity.

   Type II – deuteranopia-like, with mild to severe confusion of red-green hues with a concomitant mild loss of blue-yellow color discrimination and moderate to severe reduction in visual acuity.

   Type III – tritanopia-like, with mild to moderate confusion of blue-yellow hues with a lesser impairment of red-green color discrimination. Vision acuity in this type may be normal or moderately reduced.

It should be noted that the color tests used routinely in the ophthalmic clinic, e.g., pseudo-isochromatic plates (like Ishihara plates), Farnsworth D-15, and Farnsworth-Munsell 100-Hue tests, were designed to diagnose specifically the primary inherited color vision deficiencies that are defined physiologically. These tests are also used to define the color vision deficiency in disorders of the visual system that interfere with color vision. In the initial stages, a definition of disorder type according to Verriest is possible. However, at later stages the color vision defect is quite general and more difficult to define.

Cross-References

- ▶ Absorption, Light, Spectra of Visual Pigments
- ▶ Achromatopsia
- ▶ Achromatopsia Cerebral
- ▶ Age-Related Macular Degeneration
- ▶ Anomalous Trichromats
- ▶ Arteritic Ischemic Optic Neuropathy
- ▶ Blue Cone Monochromatism
- ▶ Color Vision, Three Cone Opsins
- ▶ Dyschromatopsia
- ▶ Inherited Color Vision Defects
- ▶ Macular Dystrophy
- ▶ Photoreceptor Cells
- ▶ Secondary Glaucoma in Uveitis/Inflammatory Eye Disease

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Color Vision Deficiency

- ▶ Achromatopsia Cerebral
- ▶ Anomalous Trichromats
- ▶ Color Blindness

Color Vision, Three Cone Opsins

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Definition

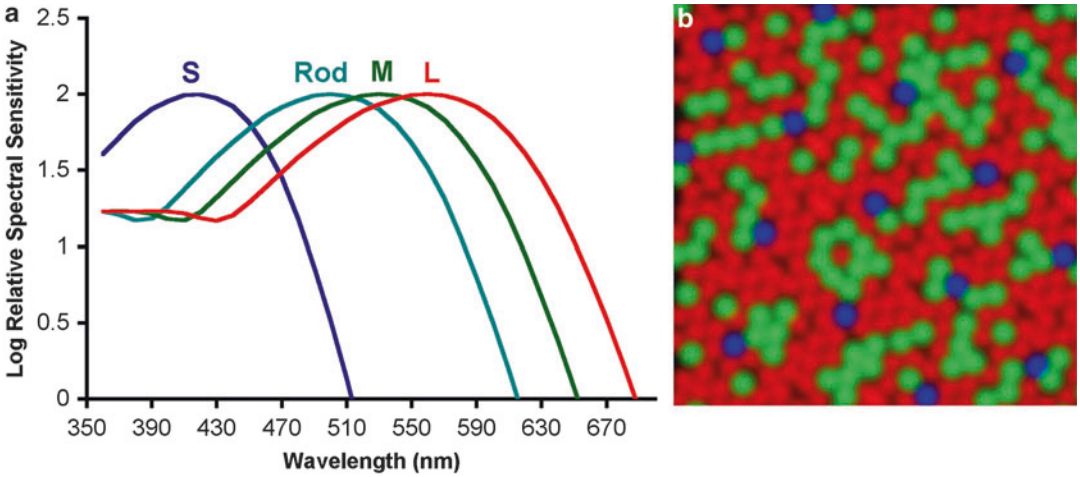
Color vision refers to the ability to discriminate objects based solely on the wavelength they reflect/emit. The presence of three distinct types of cone opsins provides humans with trichromatic color vision.

Basic Characteristics

Photoreceptor Basis of Human Color Vision

Humans with normal color vision can discriminate some two million hues. The retinal substrate for this exquisite color perception is the cone photoreceptor mosaic. While the highly sensitive rods outnumber cones nearly 20:1 and subserve vision at low (scotopic) light levels, it is the cones that underlie the majority of the visual experience at high light levels (photopic), including high spatial acuity and color vision.

There are three types of cone photoreceptors, each having a distinct spectral sensitivity (Fig. 1). The spectral sensitivity of the photopigment simply reflects the probability of it absorbing a photon of light and is determined by the particular photopigment present in the cone cell. Retinal photopigments consist of two parts: a protein (opsin) and a chromophore (in humans, 11-*cis*-retinal). The chromophore is covalently bound via a protonated Schiff base linkage with a specific lysine



Color Vision, Three Cone Opsins, Fig. 1 Photopigment basis for trichromatic color vision. (**a**) Photopigment absorption spectra. The human photopigments have different, but overlapping, spectral sensitivities. The cone photopigments, which dominate the photopic (daytime) vision are named based on the region of maximal absorption in the visible spectrum – short (*S*), middle (*M*), or long-wavelength sensitive (*L*). Rods serve scotopic vision and are maximally sensitive at about 500 nm. (**b**) Simulation of the organization of the L (*red*), M (*green*), and S (*blue*) cones within the cone photoreceptor mosaic. Note the relative paucity of S cones in the mosaic, and the random arrangement of the L & M cones, with L cones outnumbering M cones by about 2:1 in individuals with normal color vision, though this is variable

residue in the opsin (apoprotein) molecule. Opsins belong to the protein superfamily of G protein-coupled receptors (GPCR).

Three Cone Opsins

Photopigments (and their associated cones) are classified according to the region of the visible spectrum they are most sensitive to – either short-, middle-, or long-wavelength sensitive (abbreviated S, M, and L). All humans with normal color vision have the same S-cone pigment, with peak absorption around 417 nanometers (nm). The M-cone pigment varies slightly among individuals, with an average peak at about 530 nm. There is variability in the peak sensitivity of the L-cone pigment among humans with normal color vision, though there are two main variants that peak at 555 and 559 nm. Trichromatic color vision relies on the presence of one cone type from each of these three spectral classes, and these cone types appear to be randomly arranged within the cone mosaic (Fig. 1). While the human retina contains some 100 million photoreceptors, only about five million of them are cones, and of the cones, about 95% are of the L/M type. If the function of one or more of the cone classes is disrupted or absent, the result is a color vision defect.

At the protein level the L and M pigments are about 96% homologous, though they show only 43% identity with the S pigment. Since all cone photopigments employ the same chromophore (11-*cis*-retinal), the difference in spectral sensitivity between photopigments is linked directly to the opsin protein. A small number of amino acid positions within the opsin molecule are involved in spectrally *tuning* the pigment – generating the spectral difference between the S, M, and L opsins as well as the spectral variation within the M and the L pigment class.

Cross-References

▶ Absorption, Light, Spectra of Visual Pigments
▶ Color Blindness
▶ Inherited Color Vision Defects

Further Reading

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Colvard Pupillometer

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Synonyms

Hand-held infrared pupillometer

Definition

A hand-held device for measuring pupil diameter.

Purpose

Measurement of pupil diameter prior to refractive surgery or for neuro-ophthalmological purposes.

Principle

The Colvard pupillometer is a hand-held view-through residual light amplification device developed by Michael Colvard (1998). An infrared LED serves as light source that leaves the pupil diameter unaffected. The anterior segment of the patient is viewed on a light amplification screen. A ruler with a millimeter scale is superimposed over the image of the subject's eye. The examiner can measure/estimate the subject's pupil diameter directly using the ruler. A rubber cup avoids disturbing light falling into the subject's eye and affecting the pupil diameter.

Indication

Measurements of the mesopic pupil diameter are part of the preparing examinations prior to refractive surgery. Also quantification of anisocoria and measurement of pupil diameters after pilocarpine, cocaine, or pholedrine application in neuro-ophthalmology require a pupillometer.

Contraindication

Measurements with the Colvard pupillometer are noninvasive. There are no contraindications.

Advantage/Disadvantage

The Colvard pupillometer is a rather simple, handy, easy-to-use, and cost-efficient device (Schnitzler et al. 2000). Therefore, it became very popular among refractive surgeons. Main disadvantages are the dependence from the surround illuminance and from the observer. If pupil behavior should be determined under standardized, controlled illuminance conditions and if simultaneous measurements in neuro-ophthalmology are required, a binocular pupillometer with a controlled background illuminance such as the Procyon pupillometer is superior to the Colvard device (Kohnen et al. 2003).

Cross-References

▶ Pupil Center
▶ Refractive Surgery

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Coma

▶ Comatic Aberrations
▶ Congenital Ocular Motor Apraxia

Comatic Aberrations

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Synonyms

Coma

Definition

A type of monochromatic aberration with asymmetry of refractive power along an axis through the pupil center.

Basic Characteristics

Coma (*gr.* κώμη: hair, tail) typically occurs if optical systems with spherical aberration undergo decentration or if an object is imaged off-axis through such an optical system. The result is an asymmetric wedge-shaped blur figure resembling a comet or a ghost image (Chalita et al. 2004). Comatic aberrations are higher-order aberrations and cannot be corrected with sphero-cylindrical lenses. In the set of Zernike polynomials, comatic aberrations are represented by polynomials of odd order ≥ 3 with an angular frequency of -1 or 1 (e.g., Z_3^{-1} for primary vertical coma). While a small amount of vertical coma is present in the healthy eye (Salmon and van de Pol 2006), coma is elevated beyond physiological levels in eyes with keratoconus, corneal scars, cataract, pterygium, after keratoplasty, and in case of decentration of excimer laser ablations and intraocular lenses. If coma originates from the cornea, it can be corrected by rigid gas-permeable contact lenses. Also objects that are imaged off-axis in an eye with spherical aberration are distorted by comatic aberrations.

Cross-References

▶ Keratoconus

References

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Combined Trabeculectomy

▶ Phacotrabeculectomy

Combined Viscocanalostomy

▶ Phacoviscocanalostomy

Comma Sign, in Sickle Cell Hemoglobinopathies

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Synonyms

Sickle cell anemia; Sickle cell disease; SCD

Definition

A hereditary form of hemoglobinopathy in which a mutated form of hemoglobin distorts the red blood cells (RBC) into a rigid crescent shape that causes small blood vessel occlusion and low tissue oxygen levels.

Genetics

In a normal red blood cell, two α-globin subunits, two β-globin subunits, and a central heme molecule combine to form adult hemoglobin (Hb A). The β-globin gene, an oxygen transport gene, is found on the short arm of chromosome 11. Hemoglobin S (Hb S) results from a single amino acid point mutation in which valine substitutes for glutamic acid within the β-globin chain, and hemoglobin C (Hb C) results from a single amino acid point mutation in which lysine substitutes for glutamic acid in the β-globin molecule. Sickle cell disease (SCD) is transmitted through an autosomal recessive mode of inheritance. Two copies of Hb S may combine with one another (SS disease), or one copy of Hb S and another β-globin variant, such as Hb C, may combine (double heterozygous SC disease). Individuals with one copy of Hb A and one copy of Hb S are described as having the sickle cell trait, the carrier state for SCD.

Ophthalmic Clinical Features

Anterior-Segment Involvement

A clinical finding in many patients is segmentation of blood in the conjunctival blood vessels. A pathognomonic sign for sickle cell hemoglobinopathies is the comma sign, which has the clinical appearance of short, truncated, isolated, dark vascular segments. Also, segmental iris atrophy and pupil abnormalities can be seen in individuals with SCD. Iris atrophy is thought to result from sectoral ischemic necrosis resulting from occluded radial iris vessels. Hyphema in a patient with SCD and in those with sickle cell trait represents a sight-threatening emergency, as even modest elevations of intraocular pressure (IOP) have resulted in vision loss from central retinal artery occlusion or macular branch retinal artery occlusion. This is likely a mechanical phenomenon, as sickled red blood cells clog the trabecular meshwork, causing elevation in IOP.

Posterior-Segment Involvement

Optic Nerve

The optic nerve in patients with SCD may exhibit vascular changes. Dark, dilated capillaries at the optic nerve head appear as small red dots and represent precapillary arterioles plugged with sickled erythrocytes.

Macula

The macula is also susceptible to infarction from vaso-occlusive disease. The "macular depression sign" has been described as an oval depression of the bright foveal or parafoveal reflex as a result of macular thinning due to ischemic atrophy.

Angioid Streaks

Angioid streaks, breaks in Bruch's membrane, have an association with SCD, occurring in 1–2% of patients. These irregular, reddish subretinal bands are most commonly found in patients with the Hb SS genotype.

Nonproliferative Sickle Cell Retinopathy (NPSR)

The retinal findings seen in NPSR are caused by arteriolar and capillary occlusion. Anastomosis and remodeling occur in the periphery, as does the resorption of the blood in the area of the infarct.

Retinal findings of NPSR include:

- Salmon patch hemorrhages – Pinkish orange hemorrhages located beneath the internal limiting membrane (ILM), occurring after a peripheral retinal arteriolar occlusion.
- Iridescent spots – After arteriolar occlusion causes retinal hemorrhage, a small schisis cavity may develop after the intraretinal portion of the hemorrhage resolves. The cavity may contain hemosiderin-laden macrophages.
- Black sunburst lesions – Flat, stellate, or round areas of hyperpigmentation. Result when intraretinal hemorrhage tracks into the subretinal space. On histopathologic examination, black sunbursts appear as focal hypertrophy of the RPE.

Proliferative Sickle Cell Retinopathy (PSR)

PSR is one of many retinal vascular diseases in which extraretinal fibrovascular proliferation occurs in response to retinal ischemia. Whereas the neovascularization in proliferative diabetic retinopathy (PDR) generally begins postequatorially, that in PSR is located more peripherally.

PSR has been classified into five pathogenic stages:

1. Stage 1: Defined by peripheral vascular occlusion. The peripheral retina may show multiple simultaneous arteriolar occlusions.
2. Stage 2: Peripheral arteriovenular anastomoses, which appear to be dilated, preexisting capillary channels.
3. Stage 3: Preretinal sea fan neovascularization, probably the most recognizable trademark lesion of sickle retinopathy. These lesions are most commonly found in the superotemporal retina, followed by the inferotemporal, superonasal, and inferonasal quadrants. Sea fans represent true neovascularization, most of them are found at the border of perfused and nonperfused retina, and they grow toward the ora serrata.
4. Stage 4: Vitreous hemorrhage. Sea fans grow or are pulled into the vitreous chamber, and vitreous traction on the delicate neovascular fronds may cause bleeding into the vitreous.
5. Stage 5: Tractional retinal detachment (TRD). TRD develops as the result of chronic vitreous hemorrhage or chronic transudation from neovascular tissue and resultant vitreous membrane formation.

Diagnosis

Fluorescein angiography (FA) is the gold-standard imaging tool for assessment of retinal perfusion status. A potential limitation of conventional fluorescein angiography is the inability to image the pathology of the far peripheral retina in some eyes with sickle retinopathy.

Ultrawide-field fundus photography and angiography have become useful in the evaluation of the retinal periphery in eyes with sickle cell retinopathy.

Indocyanine green (ICG) angiography has been studied as a way to assess choroidal perfusion, but the utility of ICG in sickle retinopathy is as yet undetermined.

Optical coherence tomography (OCT) may provide important details about foveal anatomy, which may aid in the diagnosis and management of sickle retinopathy even in asymptomatic patients.

Therapy

Treatment of PSR may be considered in the eye of an individual with significant visual loss from PSR or vision impairment in the contralateral eye. Treatment may also be required in cases of rapid growth of a sea fan, presence of large, elevated sea fans, spontaneous hemorrhage, or bilateral proliferative disease. The goal of intervention is to prevent the progression of stage III to stages IV and V.

Scatter laser photocoagulation is the current mainstay of treatment in PSR. The objective of scatter laser treatment is similar to that employed in the management of PDR. Anti-VEGF agents have been reported to cause complete regression of retinal neovascularization and resolution of vitreous hemorrhage following intravitreal injection in eyes with PSR, but further study is warranted to assess its role in treating PSR. Vitrectomy may be considered for nonclearing vitreous hemorrhage or TRD. Exchange transfusion, erythropheresis, and hyperbaric oxygen have been attempted to minimize complications from surgically induced anterior-segment ischemia. These methods were without clear benefit and were associated with systemic complications.

Epidemiology

Sickle cell disease (SCD) is the most common inherited blood disorder and affects nearly 80,000 people of African-American and Hispanic descent. SCD occurs in 0.2% of African American births and in 0.0027% of Hispanic-American births. Approximately 8% of African Americans possess sickle cell trait, which is not associated with increased mortality or morbidity. At-risk genotypes for SCD are also observed in people of Mediterranean, Caribbean, South and Central American, Arab, and East Indian descent.

Further Reading

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Schubert HD (2013) 2013–2014 basic and clinical science course, section 12: retina and vitreous. American Academy of Ophthalmology, San Francisco

Common Tendinous Ring

► Annulus of Zinn

Common Wart

► Verruca Vulgaris

Commotio Retinae (Berlin Disease/Edema)

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Synonyms

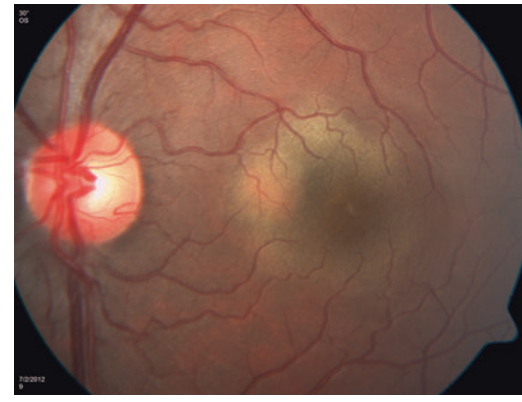
Berlin's edema; Retinal concussion; Retinal contusion; Traumatic retinopathy

Definition

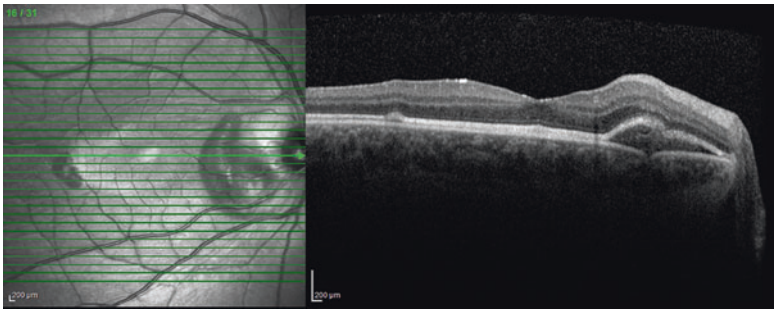
A gray-white change in color of the retina following a blunt contusion. The pathology affects primarily the outer retinal layers. When confined to the macular area, the condition is called Berlin's edema, a term first introduced by Berlin in 1873 (Agarwal 2012) (Figs. 1 and 2).

Etiology

After a blunt trauma to the globe, swelling and disorganization of the outer retinal layers ensue, causing an opaque and whitened look to the retina area involved. Retinal whitening usually appears a



Commotio Retinae (Berlin Disease/Edema), Fig. 1 Color fundus image of Berlin's edema macular commotio retina



Commotio Retinae (Berlin Disease/Edema), Fig. 2 OCT image of a combined Berlin's edema and choroidal rupture case. Sub-foveally there is hyperreflectivity of the IS-OS junction. Nasally there is an elevation of the RPE and a focal defect in Bruch's membrane, corresponding to the choroidal rupture seen on the infrared picture

few hours after the insult. The swelling occurs at the outer retinal layers.

The injury is presumably mechanical, with deformation of the vitreous and hydraulic forces shift as a result of the injury, traversing the globe and damaging the retina. Commotio retina is presumably a contrecoup injury to the retina, i.e., occurs at the side opposite that of the impact site. There are also reports of a hemodynamic component to the injury, but these are less prominent.

Histopathologic studies showed that the whitening is caused by fragmentation of the photoreceptor outer segments and acute damage to the photoreceptor cells. Other histopathological features include edema of Muller cell processes and of the retinal ganglion cell axons and retinal pigment epithelium (RPE) damage. Commotio retina is not a "true" edema, as little extracellular fluid accumulation occurs.

Whitening of the retina is believed to occur because of the loss of the vertically oriented configuration of the photoreceptor tips, into a disarrayed mesh and consequent loss of regular light scatter.

Clinical Presentation

Patients present after blunt ocular trauma, with a decrease in vision which varies between 20/20 and 20/400, depending on the region of the retina involved and the extent of the damage. The severity of the decrease in vision does not always correlate with the degree of retinal opaqueness.

When presenting early after injury, the retinal examination may appear normal although the patient complains of decreased vision. A period of spontaneous resolution follows; its duration depends on the extent and severity of the initial damage. Mild commotio retina usually resolves after a few days, while more severe cases can show a prolonged course of a few months, some with residual non-resolving sequelae.

Diagnosis

No laboratory tests are contributory to the diagnosis, as the diagnosis is mainly made following a suggestive history and careful clinical examination.

Different imaging modalities aid in better categorizing and assessing the insult: visual field testing, especially microperimetry testing, is useful in demonstrating small visual field defects which might develop after photoreceptor cell death.

Fluorescein angiography (FA) shows in cases of mild commotio retina areas of hypofluorescence in the areas of opaque retina; mild RPE staining is sometimes seen, and no leakage from the retinal vessels. In more severe cases, FA demonstrates a more intense staining and occasional leakage of retinal vessels, corresponding to the more extensive damage at the RPE level.

Multifocal electroretinogram (mfERG) demonstrated reduced sensitivity in involved areas, which improves with resolution of the commotio retina. Some studies show reduced retinal

sensitivity even after complete OCT resolution and restored visual acuity, suggesting lasting damage despite complete functional resolution.

OCT imaging aids in better visualization of mainly macular commotio retina (Ahn et al. 2013). Several features are visible upon imaging and include, with escalating severity:

1. Inner segment–outer segment (IS-OS) junction hyper-reflectivity
2. Cone outer segment tip (COST) defects
3. COST and IS-OS junction defects
4. COST, IS-OS junction, and external limiting membrane (ELM) defects

Prognosis seems to worsen with increasing severity of OCT findings.

Differential Diagnosis

In the absence of adequate history, retinal whitening in certain configurations can resemble branch retinal artery occlusion or cilioretinal artery occlusion. The retinal thickening however occurs at different retinal levels and is mainly affecting the inner retinal layers in vascular occlusions as opposed to affecting the outer retinal layers in commotio retina.

Prophylaxis

The main prophylactic measure is the prevention of ocular trauma, by either using a protective eye wear or by avoiding harmful circumstances.

Therapy

No known intervention is currently known to alter commotio retina course or prognosis. Common pathologies occurring in conjunction with commotio retina need to be actively sought out in order to administer appropriate therapy and readily convey prognosis. These include retinal tears, dialysis, choroidal rupture, retinal detachment, and traumatic optic neuropathy.

Prognosis

When uncomplicated, commotio retina is usually a self-limited disease (Blanch et al. 2013). In patients presenting with an extramacular commotio retina, the visual prognosis is excellent, with resolution of the retinal whitening after a few days. Macular commotio retina cases present with a more varied prognosis, and while the majority shows an improvement in visual acuity to pre-injury levels, some cases show prolonged recovery over 3 months, a decrease from pre-injury visual function, and persistent scotoma. As mentioned above, several OCT features visible soon after injury are helpful in better assessing future visual recovery. Injury limited to the IS-OS junction and COST usually holds good visual rehabilitation and visual acuity restoration to pre-injury or near pre-injury levels. A more severe macular commotio retina showing ELM defects can later show RPE atrophy and photoreceptor defects leading to decreased visual outcomes and visual field defects.

Cases complicated by subfoveolar hemorrhage, macular hole, or choroidal rupture may show poorer visual acuity outcomes, determined mainly by the extent of the additional pathology and resultant complications.

Epidemiology

Commotio retina is a relatively common disease, accounting for 0.4% of civilian (Weichel et al. 2008) and 15% of military eye injuries. It is more common in young men, as with other trauma-related injuries.

Cross-References

- ▶ Macular Holes
- ▶ Optical Coherence Tomography
- ▶ Retinal Tears
- ▶ Vitreous Humor

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Weichel E, Colyer MH, Ludlow SE, Bower KS, Eiseman AS (2008) Combat ocular trauma visual outcomes during operation Iraqi and enduring freedom. Ophthalmology 115(12):2235–2245

Communicating Arteries Anterior

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Synonyms

Anterior communicating artery

Definition

The anterior communicating artery is a very short artery in the circle of Willis, a hexagon of vessels that anastomoses the major blood supplies of the brain. The anterior communicating artery connects the left and right anterior cerebral arteries, allowing for communication to both hemispheres of the brain. This is particularly important should the internal carotid artery become occluded on either side.

Cross-References

▶ Aneurysms

Further Reading

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Complex Microphthalmia

▶ Microphthalmos (Microphthalmia), Anterior

Complex Visual Hallucination

▶ Charles Bonnet Syndrome: Overview

Complexion-Associated Melanosis

▶ Ephelis (Freckle), Conjunctival Disease
▶ Pigmented Lesions of the Conjunctiva

Compound Nevus

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Synonyms

Acquired melanocytic nevus; Melanocytic nevus

Definition

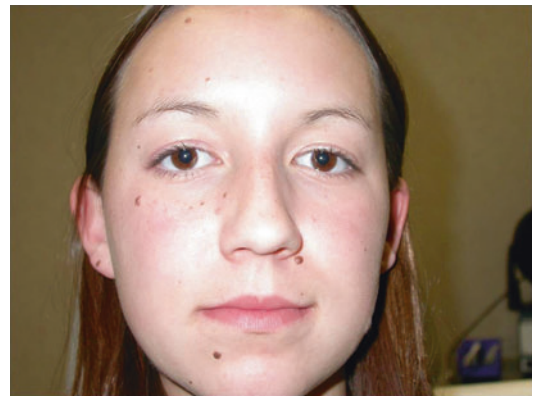
A benign neoplasm composed of nests of melanocytes located on the dermoepidermal junction and dermis layers of the skin (Albert and Jakobiec 2008; Shields and Shields 2008).

Etiology

Unknown. A genetic factor is likely in many families, working together with sun exposure. They may occur on the eyelid skin and on the eyelid margins. Lesions typically present in childhood as small, flat, tan macules that increase in size on the basal epithelium. As the lesion increases in diameter, a nest of cells drops of into the dermis; later, the cells migrate entirely in the dermis (intradermal nevus). Therefore, the natural progression from junctional nevus to compound nevus, then to intradermal nevus is consensus.

Clinical Presentation

Domed pigmented (light or dark brown) nodules are of up to 1 cm in diameter (Fig. 1). The borders of the lesion are irregular but symmetric. Most lesions are smooth, but larger ones may be cerebriform, or hyperkeratotic and papillomatous; hairs may be present.



Compound Nevus, Fig. 1 Pigmented melanocytic nevis involving the periocular region

Diagnostics

Clinical presentation. Histopathologic evaluation is confirmatory to compound nevus.

Differential Diagnosis

Differential Diagnosis includes ▶ melanoma, ▶ seborrheic keratosis, ▶ neurofibroma, and ▶ atypical nevus.

Prophylaxis

Avoidance of sun exposure and sun education.

Therapy

The majority do not require treatment and can be observed periodically. Indications for removal include cosmetic concerns, chronic irritation

(itching and/or bleeding), and changes in appearance (color, size, or shape) that are suspicious for melanoma. Options of surgical therapy when the lesion involves eyelids include shave biopsy, excisional biopsy, or full thickness eyelid biopsy.

Prognosis

Most are benign with little malignant potential. The most active nevus is the junctional nevus. As nevi descend further into the dermis (compound and intradermal nevi), they decrease in potential to malignant transformation.

Epidemiology

The prevalence of melanocytic nevus varies with age and race. They increase in number gradually during childhood and adolescence, reaching a peak during adult life and declining with increasing age. These lesions are common in patients with light or fair skin (Albert and Jakobiec 2008; Shields and Shields 2008).

Cross-References

- ▶ Choroidal and/or Ciliary Body and/or Iris Melanoma
- ▶ Excisional Biopsy
- ▶ Full-Thickness Eyelid Biopsy
- ▶ Intradermal Nevus
- ▶ Junctional Nevus
- ▶ Neurofibromas, Discrete

References

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Computerized Corneal Topography

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Synonyms

Anterior segment optical coherence tomography; Corneal mapping; Corneal tomography; Photokeratoscopy; Photovideokeratoscopy; Posterior corneal mapping; Scheimpflug imaging; Videokeratography

Definition

Noninvasive medical imaging technique of the cornea to determine corneal power.

Purpose

To map the curvature of the cornea.

Principle

Corneal topographic measurements can be either derived from the slope of the cornea or directly measured from elevation data (Swartz et al. 2007). Most commonly, slope data is examined through the use of a pattern of illuminated, concentric rings focused onto the anterior surface of the patient's cornea with the concentric rings and then reflected back to a digital camera. Several thousand data points are generated via the reflected pattern allowing for corneal curvature to be calculated based on the spacing between rings. The topographical map is then produced and color-coded based on steepness or dioptric power of the cornea. These measurements,

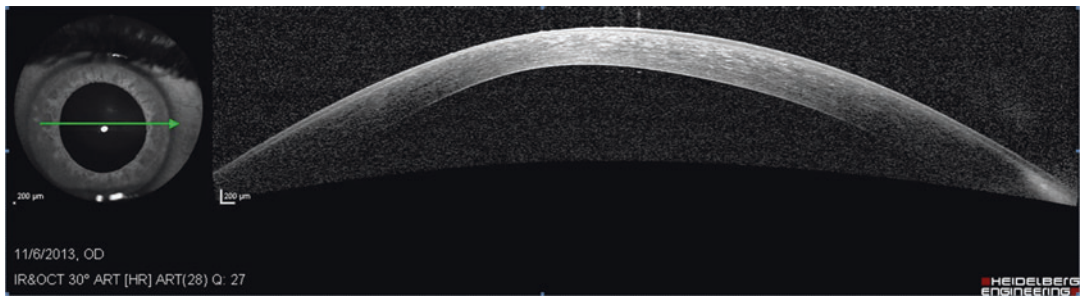
however, assume a normal posterior corneal curvature and, therefore, power (Fowler and Dave 1994; Martinez and Klyce 2010). Newer techniques, such as the slit scanning technology used in the Orbscan (Bausch & Lomb, Rochester NY) and Scheimpflug imaging used in the Pentacam (Oculus, Arlington WA), more directly measure elevation data (Martinez and Klyce 2010). The techniques use a series of slit beams at regular intervals but variable angles to measure the curvature and regularity of the anterior and posterior corneal surface, as well as corneal thickness to generate a complete reconstruction of corneal anatomy. Pentacam technology, in particular, uses Scheimpflug optics to vary the depth of focus, generating thousands of elevation points and 25 or 50 images to create a three-dimensional representation of the cornea. There are many different indices used to aid calculation of corneal surface regularity. Direct imaging of the anterior and posterior cornea is also possible using anterior segment optical coherence tomography (ASOCT). ASOCT uses the emission and reflection of light, similar to ultrasound technology, to build a cross-sectional image of the cornea, including corneal thickness (Heur et al. 2010).

Indication

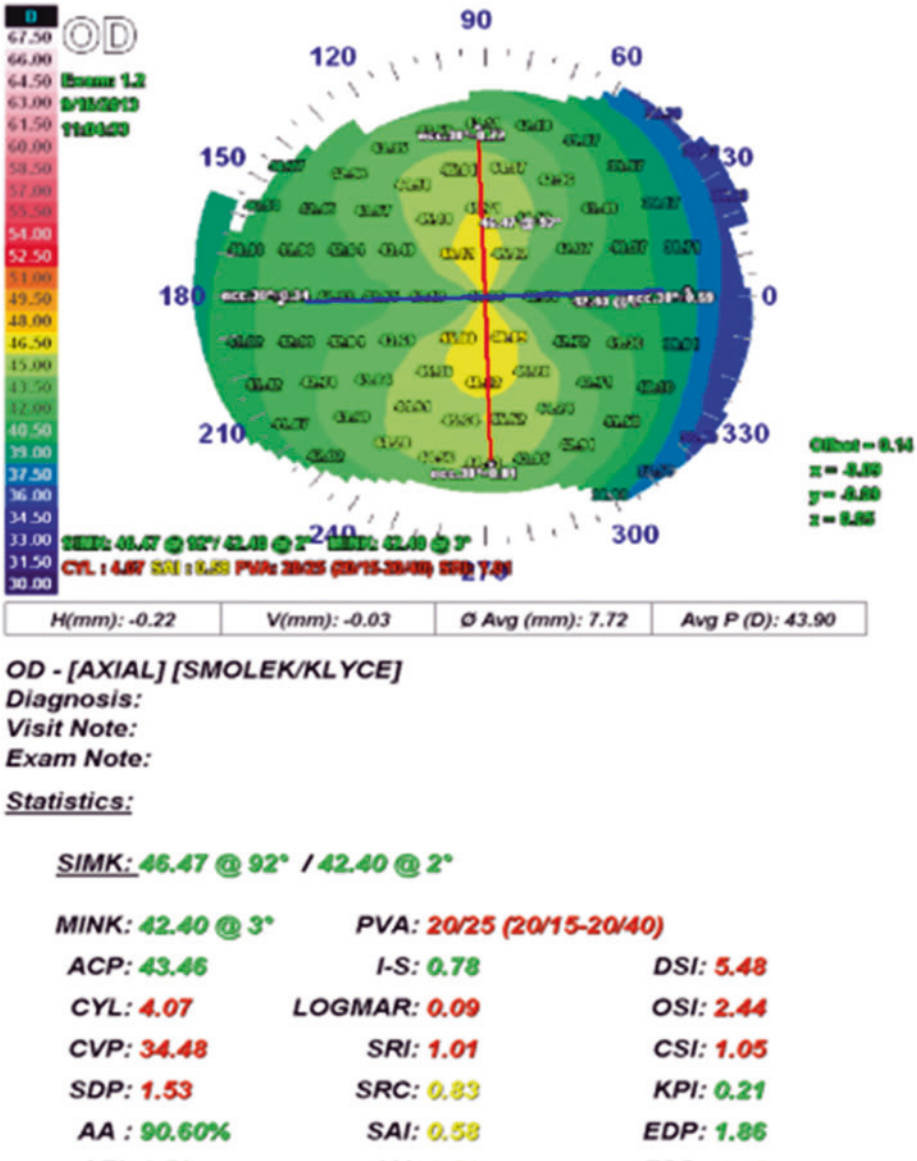
Computerized corneal topography can be a useful diagnostic procedure when evaluating for corneal ectatic disease including keratoconus or pellucid marginal degeneration (Martinez and Klyce 2010) (Fig. 1). Topography can also provide useful preoperative measurements for any patient requiring refractive surgery or cataract surgery patients to aid in intraocular lens implant selection. Any patient with a significant degree of astigmatism postoperatively can also benefit from topography to guide further management (Fig. 2). Finally, patients who require rigid gas permeable contact lens can benefit from topographical measurements to ensure optimal contact lens fit.

Advantage/Disadvantage

Computerized corneal topography is a noninvasive, quick measurement with results that are generally operator and patient independent. Patients with both "forme fruste" (i.e., subclinical) and clinical keratoconus can benefit from corneal topography to evaluate severity of disease as well as to guide future management. ASOCT can be quite useful in managing patients with corneal opacities since pachymetry can be more readily acquired versus slit scanning technology (Heur et al. 2010). Topography and ASOCT are less affected by the microsaccadic movements of the eye secondary to rapid acquisition time, whereas scanning slit technology and Scheimpflug imaging can produce inconsistent results given longer acquisition times. A disadvantage of corneal topography is that data points are based on patterns of reflection from the surface of the eye; therefore, a smooth, healthy ocular surface is necessary. Surface eye disease, e.g., dry eye syndrome, epithelial defect



Computerized Corneal Topography, Fig. 1 Anterior segment OCT of the right eye of a patient with keratoconus shows paracentral thinning



Computerized Corneal Topography, Fig. 2 Topography of the right eye of a patient displays the classic "bow tie"-shaped pattern of regular, with-the-rule astigmatism

can result in unreliable and inaccurate results (Swartz et al. 2007).

Cross-References

- ▶ Ectasia, Corneal
- ▶ Pellucid Marginal Degeneration
- ▶ Photokeratoscopy

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Computerized Videokeratography

► Corneal Topography

Concretions

► Conjunctival Degenerations

Concretions, Conjunctival

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Synonyms

Conjunctival lithiasis

Definition

Small, superficial, subepithelial deposits white to yellow in color found in the palpebral conjunctiva, usually in elderly patients or those with chronic conjunctivitis. Histopathologically, they are epithelial inclusion cysts filled with epithelial and keratin debris. Secondary calcification of concretions can occur, in which case they are referred to as conjunctival lithiasis. Usually asymptomatic, concretions may cause foreign-body sensation if they lead to erosion of the overlying epithelium, in which case they can be removed at the slit lamp under topical anesthesia.

Cross-References

► Lithiasis, Conjunctival

Concussion

► Concussive Trauma

Concussive Trauma

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Synonyms

Concussion; Mild head trauma; Mild traumatic brain injury (MTBI); Minor closed head injury

Definition

A concussive trauma, or mild traumatic brain injury (MTBI), is caused either by non-penetrating contact injuries to the head or neck or by the force of rapid acceleration or deceleration. While there is no clear consensus on the clinical definition of a concussive trauma, several organizations, including the World Health Organization (WHO) and the American Congress of Rehabilitation Medicine, have published MTBI definitions. They agree that concussion results in a transient impairment in neurologic functions that occurs shortly after a traumatic incident. Neurologic impairments include loss of consciousness, posttraumatic amnesia, altered mental status, and focal neurological deficits, including neuro-ophthalmologic deficits such as pupil dysfunction, traumatic optic neuropathy, ocular motility dysfunction, and visual disturbances. To be considered a mild traumatic brain injury, the loss of consciousness cannot exceed 30 min, and the posttraumatic

amnesia cannot exceed 24 h (Bodin et al. 2012). The WHO further defines an MTBI by a Glasgow Coma Scale score of between 13 and 15 at approximately 30 min post-injury.

Etiology

Concussive trauma results from blunt force to the head, with either the head colliding with an object or an object forcibly hitting the head. Common causes include falls, sporting injuries, and motor vehicle accidents. Concussive trauma can also result from acceleration or deceleration forces, when the head moves or stops suddenly and rapidly, as in a car accident. Blast injuries from military explosions are another cause of concussive trauma. The most common causes of MTBI are motor vehicle accidents (Albert et al. 2008). In all cases, concussion depends upon the sudden motion of a stationary head or the halting of a moving head. As the cranium and its overlying structures move, so too does the brain, suspended in cerebrospinal fluid. Depending on the location and angle of the trauma upon the head, the brain can undergo linear acceleration, rotational acceleration, angular acceleration, or a combination. The exact mechanism of the resultant clinical syndrome – loss of consciousness, posttraumatic amnesia, altered mental status, and focal neurological deficits – is widely debated. Interference with the reticular activating system is postulated to account for the loss of consciousness often seen in concussive trauma. Other hypotheses for the pathophysiology of MTBI include interference with the cholinergic reticular inhibitory system and neuronal paroxysmal depolarization shifts resulting in a convulsive process (Moore et al. 2012).

Clinical Presentation

The four primary presentations of concussive trauma patients are loss of consciousness, posttraumatic amnesia, altered mental status, and focal neurological deficits. Patients may present with one, some, or all of these conditions. Some, but not all, of concussion patients experience loss of consciousness, and in MTBI, this loss of consciousness is short-lived. Patients rapidly transported to a hospital emergency department following a closed head trauma may present unconscious, or EMS and/or accompanying family or friends may report a history of loss of consciousness. Posttraumatic amnesia is a state of confusion and an inability to store new memories in the moments after a concussive trauma. This amnesia, combined with altered mental status and loss of consciousness, can make it difficult to obtain information from the patient, such as identifying information, a medical history, and a narrative of what occurred during the actual trauma. Altered mental status includes confusion, disorientation, and attention deficits. This can manifest as incoherent or repetitive speech, mental sluggishness, or inability to respond to questions. Focal neurological deficits refer to impairments of specific nervous system functions and include disordered movement, paralysis, cognitive impairment, and sensory impairment. Patients also commonly experience headache following a concussive trauma; other potential symptoms include difficulty with balance and coordination and concussive convulsions (brief tonic-clonic movements).

The sensory impairments that can occur following a concussive trauma include a variety of neuroophthalmic manifestations. Traumatic mydriasis is dilation of the pupil that occurs as a result of injury to the iris sphincter. It is usually unilateral, and the affected eye will constrict poorly to light and accommodation.

If the trauma damages the sympathetic nervous system pathway anywhere from the hypothalamus to the eye, the patient will present with Horner syndrome, which includes miosis and ptosis on the affected side. Depending on where in the pathway the lesion is, the patient may also present with anhidrosis and dilated conjunctival blood vessels on the affected side.

Traumatic optic neuropathy (TON) results when the optic nerve is damaged, most commonly when the force of a blunt head trauma is transmitted to and damages the optic nerve. Patients with TON present with unilateral visual loss, defects in

color vision, and/or a relative afferent pupillary defect (RAPD). In some patients, the RAPD is the only presenting sign of TON, highlighting the importance of a complete opthalmic examination in head trauma patients (Kanski 2009).

Damage to any part of the visual pathway will result in accompanying visual field defects. As one example, traumatic chiasmal injury typically produces bitemporal hemianopia. Any traumatic lesion of the anterior visual pathway (retina, optic nerve, chiasm, or optic tract) will also cause an RAPD.

Although more common in severe head trauma, mild head trauma can also damage the cranial nerves. When the third, fourth, or sixth nerves are injured, opthalmic symptomatology results. A patient with damage to the oculomotor nerve (third nerve palsy) will present with diplopia, ptosis of the affected eyelid, mydriasis, and motility deficits. Due to loss of innervation of the superior, medial, and inferior rectus, as well as the inferior oblique, adduction, depression, and elevation of the affected eye will be impaired on physical exam. Due to its long length, the trochlear nerve is particularly susceptible to traumatic injury. Patients with fourth nerve palsy often present with a head tilt to the contralateral side as well as diplopia that is worsened by looking downward. On exam, they have impaired ability to depress the eye in adduction. The head tilting occurs to compensate for the loss of superior oblique muscle function in the affected eye. Injury to the abducens nerve is uncommon except in serious head trauma. Sixth nerve palsy presents with diplopia, impaired abduction due to the loss of function of the lateral rectus muscle, and esotropia (Schiefer et al. 2007).

Diagnosis

The diagnosis of MTBI is largely a clinical one. A history of trauma to the head or neck, combined with the clinical presentation of loss of consciousness, altered mental status, posttraumatic amnesia, and/or focal neurologic deficits, is highly suggestive of a concussion. In the acute setting following injury, computed tomography is the imaging modality of choice for most patients in order to evaluate for the presence of fracture or hemorrhage.

In order to evaluate for any opthalmic manifestations, a full examination of the eyes should be performed, including assessment of the size and shape of the pupils, symmetry between bilateral pupils, pupillary response to light and accommodation, and assessment for a potential RAPD. Eye examination should also include assessment of the patient's visual acuity, visual fields, color vision, and ocular range of motion.

Unilateral mydriasis can result from pupillary sphincter injury, such as small tears to the sphincter muscle caused by the traumatic injury, or from trauma-induced damage to the oculomotor nerve (CN III). Unilateral miosis suggests that there is a lesion somewhere in the sympathetic nervous system pathway, causing Horner syndrome. A patient with Horner syndrome will additionally present with diplopia, ptosis of the affected eyelid, impaired adduction, depression, and elevation of the affected eye and may present with anhidrosis and dilated conjunctival blood vessels on the affected side.

Injury to the trochlear nerve (CN IV) and the abducens nerve (CN VI) will also cause diplopia and ocular motility dysfunction. Specifically, a patient with trochlear nerve damage will have difficulty depressing the affected eye in adduction, and the diplopia is worsened by looking downward. Fourth nerve palsy also presents with a compensatory head tilt toward the unaffected side in order to compensate for the lost ocular motility. A patient with abducens nerve injury will have impaired ability to abduct the affected eye and may present with esotropia, with the eye turning medially.

A relative afferent pupillary defect (RAPD), during which both pupils constrict when light is shone into the unaffected eye and both pupils dilate when the light is swung into the damaged eye, reflects a lesion anywhere in the anterior visual pathway or traumatic optic neuropathy (TON). Changes in visual acuity or visual fields that accompany an RAPD are suggestive of TON, while isolated visual changes are caused by lesions of the visual pathway. In TON,

fundoscopic examination is initially normal following the traumatic injury, so a patient presenting immediately or shortly after a concussive trauma will have a normal-appearing fundus even if traumatic optic neuropathy has occurred. Optic atrophy and optic disc pallor are not visualized on fundoscopic examination until approximately 3–6 weeks after the inciting trauma.

Differential Diagnosis

A history of trauma, such as a motor vehicle accident, a sports injury, or a witnessed fall, is highly suggestive of an MTBI as the cause of the presenting symptoms of loss of consciousness, posttraumatic amnesia, altered mental status, and/or focal neurological deficits. If a traumatic injury cannot be confirmed by either the patient or a witness and there is no physical evidence of a trauma (such as contusions, lacerations, ecchymosis, or edema), toxicology should be performed to rule out drug or alcohol overdose as the causative agent of the symptoms. Even if drug and alcohol toxicology is positive, MTBI remains on the differential, as an intoxicated patient could have suffered a concussive trauma and the symptomatology of intoxication and MTBI may be overlayed.

Unilateral mydriasis can be caused either by pupillary sphincter injury or by oculomotor nerve damage, both of which can result from a concussive trauma. If the patient also presents with ipsilateral ptosis and ocular misalignment, the unilateral mydriasis is likely to be a result of a third cranial nerve lesion. Isolated unilateral mydriasis without other opthalmic manifestations is more likely to be caused by tears in the pupillary sphincter muscle. The diagnosis can be confirmed using pharmacologic testing with 1% pilocarpine, as a pupil with sphincter damage typically fails to constrict in response to pilocarpine.

Unilateral miosis is suggestive of Horner syndrome (damage to the sympathetic nervous system pathway), but bilateral miotic pupils are more commonly caused by narcotic use and further point to the value of obtaining toxicology.

Prophylaxis

The primary prophylactic measure to prevent concussive traumas is accident prevention. As motor vehicle accidents are a common cause of mild traumatic brain injury, automotive safety interventions such as seat belts and air bags are key to preventing such injuries. These interventions can be enacted on the federal and state governmental level, including the drafting of laws that govern speed limits and safe driving, the regulation of the safety features of automotives, and the enforcement of vehicular laws by police officers. Safety interventions are also enacted by the motor vehicle industry in the manufacturing of safety interventions such as seat belts, alarms that indicate a driver or passenger is not buckled, air bags, and roll-over prevention mechanisms. Finally, individual drivers should be educated on the importance of practicing safe driving habits such as using a safety belt, obeying the speed limit, and obeying traffic laws to prevent motor vehicle accidents.

Sports injuries are another common cause of MTBI. Concussive traumas to the head can be mitigated by the use of helmets and/or protective gear as well as by the enforcement of rules that limit contact forces to the head and neck. Falls, especially in the elderly population, also commonly result in MTBIs. Elderly individuals, as well as anyone else at increased risk of falls, can reduce fall risk by wearing supportive shoes, eliminating clutter in hallways and passageways, and assuring adequate lighting. Hospitalized patients are particularly at risk for falls, so patients should be assessed for their fall risk upon admission to the hospital. If a patient is at risk for fall, interventions such as coiling excess electrical wires, ensuring the call button is easily accessible, and clearing the pathway to the bathroom can be employed to reduce the risk of a fall and thus an MTBI or other injuries.

Therapy

MTBIs are generally managed conservatively, with observation and rest as the cornerstones of

treatment. The symptoms of a concussive trauma (altered mental status, amnesia, focal deficits) should abate on their own over the course of approximately 1–2 weeks. Patients are monitored to ensure that symptoms do indeed resolve, but worsening or persistence of symptoms merits additional workup and care. During the 1–2 weeks post-concussion, patients should rest both physically and cognitively, avoiding any strenuous physical or mental activity and especially avoiding any activities, such as contact sports, that could predispose the patient to suffering another head injury.

If the concussive trauma causes a traumatic optic neuropathy (TON), potential therapies include observation, corticosteroids, and surgical decompression of the optic canal, although therapeutic management of TON is controversial. Current treatment protocol begins with high-dose intravenous methylprednisolone therapy: a 30 mg/kg loading dose infused over a minimum of 30 min and followed by a maintenance dose of 5.4 mg/kg/h for 48 h (Albert et al. 2008). The therapeutic response to corticosteroids is then monitored by continually retesting for the presence of an RAPD and assessing the patient's visual acuity and visual fields. If the intravenous methylprednisolone results in improved function for the patient after 48 h, therapy should be switched to oral prednisone therapy and should be tapered. If there is no improvement after 48 h, corticosteroids should be continued for up to 72 h. If there is no improvement after 72 h, surgical decompression of the optic canal should be considered.

Third, fourth, and sixth cranial nerve palsies caused by concussive trauma oftentimes recover spontaneously over weeks to months, so patients' symptoms of diplopia, ocular motility dysfunction, and, in the case of third nerve palsy, ptosis should be monitored over the course of several months. If deficits are still present 6 months after the inciting injury, they are more likely to persist and become comitant deviations, in which the distance between the double images of the diplopia is little affected by the direction of gaze. In the short term while the patient is being observed, patching one eye can help alleviate diplopia. If symptoms persist after 6 months, prism therapy (whereby a prism is ground into a spectacle lens) can be used to mitigate visual symptoms. For patients who fail prism therapy, the next therapeutic option is surgery to correct strabismus. Surgery is also considered to correct the ptosis of persistent third nerve palsies.

Prognosis

The prognosis for concussive traumas is generally very good. MTBI has an extremely low mortality rate, and most of the symptoms of MTBI resolve spontaneously over the course of approximately 1–2 weeks. Problems may persist beyond this 2-week period, which reinforces the importance of observation and follow-up for patients who suffer a concussive trauma, but even in these patients, the problems are rarely permanent. Patients who have suffered an MTBI are, however, at an increased risk of suffering another concussion, most especially in the time period when they are recovering from the initial event, underscoring the importance of avoiding situations where another traumatic incident is likely to occur in the period following the concussion. The neuroophthalmic manifestations of concussive trauma also oftentimes resolve spontaneously, although these symptoms can last for longer periods of time, up to 6 months.

Epidemiology

Concussive traumas are extremely common, with an estimate of approximately 1.6 million head injuries occurring annually in the United States alone (Albert et al. 2008). There is a male preponderance in the incidence of MTBI. Concussive traumas affect people of all ages, ranging from birth to death. The most common cause of concussive trauma is motor vehicle accidents, but other common etiologies include sports injuries, falls, and assaults. Sports injuries are a particularly common cause of concussion in children, accounting for more than half of pediatric cases (Bodin et al. 2012).

Cross-References

- ▶ Anisocoria: Big Pupil
- ▶ Anisocoria of Small Pupil: Horner Syndrome
- ▶ Chemical Injury (Burns)
- ▶ Fourth Nerve Palsy
- ▶ Monocular Diplopia
- ▶ Penetrating Injuries
- ▶ Thermal Injury: Overview
- ▶ Third Nerve Palsy
- ▶ Toxic/Nutritional and Hereditary Optic Neuropathy

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Conductive Keratoplasty

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Definition

Surgical technique for the correction of hyperopia and hyperopic astigmatism and management of presbyopia by delivering radio-frequency current directly into the corneal stroma.

Purpose

Conductive keratoplasty is a non-laser treatment for presbyopia and spherical hyperopia.

Principle

Conductive keratoplasty is performed by transferring radio-frequency energy through the corneal stroma. The result is a localized heating of collagen and shrinking of collagen fibers. The curvature of the central cornea is increased and hyperopia decreased.

Indication

Patients 40 years of age or older, treatment of spherical hyperopia +0.75 to +3.25 D, temporary induction of myopia to improve near vision in the nondominant eye and presbyopic hyperopes.

Contraindication

Patients under the age of 40 and patients with myopia are not suited for conductive keratoplasty.

Advantage/Disadvantage

Conductive keratoplasty preserves the central cornea and has no flap-related complications. So far no disadvantages of the procedure have been reported.

Cross-References

- ▶ Astigmatism
- ▶ Limbal Relaxing Incisions

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Cone Degeneration

► Cone Dystrophies/Degeneration

Cone Dystrophies/Degeneration

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Synonyms

Cone degeneration; Inherited cone dysfunction

Definition

The cone dystrophies are a heterogeneous group of inherited retinal disorders, characterized by the abnormal function of the cone cells – the photoreceptors responsible for day and color vision.

They are all characterized by bilateral visual loss, color vision abnormalities, central scotomata, variable degrees of nystagmus, and photophobia, with electrophysiological or psychophysical evidence of abnormal cone function. Electroretinography (ERG) demonstrates generalized cone system dysfunction with either no (cone dystrophy) or mild rod system involvement (cone-rod dystrophy).

Disorders of cone function can be divided into stationary (cone dysfunction syndromes) and progressive disorders (cone and cone – rod dystrophies). In progressive cone dystrophies, onset is usually in childhood or early adult life, and patients often develop rod photoreceptor dysfunction in later life, thereby leading to considerable overlap between progressive cone and cone-rod dystrophies.

The stationary subtypes (such as "blue cone monochromatism" and "rod monochromatism" (achromatopsia)) which are congenital with normal rod function are described in other chapters. This chapter will focus on the progressive cone dystrophies.

Etiology

There is considerable clinical and genetic heterogeneity. Cone dystrophies (CDs) showing autosomal dominant (AD), autosomal recessive (AR), and X-linked recessive (XL) inheritance have all been reported, but the AR form is by far the most common. The genetic causes of the AD and XL inheritance have been largely clarified, but the genetic causes of the AR form are mostly unknown.

Autosomal dominant cone or cone-rod dystrophy identified and mapped genes are AIPL1, CRX, GUCA1A, GUCY2D, PITPNM3, PROM1, PRPH2, RIMS1, SEMA4A, and UNC119. While mapped loci, still unidentified, are CORD4, CORD17, and RCD1.

Autosomal recessive cone or cone-rod dystrophy identified and mapped genes are ABCA4, ADAM9, C21orf2, C8orf37, CACNA2D4, CDHR1, CERKL, CNGA3, CNGB3, CNNM4, KCNV2, PDE6C, PDE6H, RAB28, RAX2, RDH5, RPGRIP1, and TTLL5, with an unidentified locus CORD8.

X-linked cone or cone-rod dystrophy identified and mapped genes are CACNA1F and RPGR, with an unidentified locus COD2.

Findings

The progressive cone dystrophies are not usually symptomatic until late childhood or early adult

life. The age of onset of visual loss and the rate of progression show wide variability in the different families, but visual acuity usually deteriorates over time to the level of 6/60 or counting fingers.

Patients usually complain of light sensitivity and tend to see better at dusk or in the dark. Most have subnormal vision, dark to light adaptation problems, and loss of hues and color saturation. Some patients may have "urban night blindness"; in a city environment, there is usually enough light at night so the rods are unable to undergo full dark adaptation, while cones do not function as well. Congenital or early cases will typically have nystagmus.

Common fundus findings include bull's eye maculopathy and profound macular atrophy with a "cookie cutter" shape, while some cases show only subtle atrophic RPE changes and granularity or a normal looking macula.

In most patients the atrophy is confined to the fovea and usually is symmetric between eyes. Temporal optic pallor or atrophy is common. The retinal periphery is usually normal in pure cone dystrophies, although rarely white flecks similar to those seen in fundus flavimaculatus may be seen. Some X-linked cone dystrophy patients have confluent retinal areas of tapetal-like sheen, and rare patients have crystal deposits in the macula. Abnormal retinal blood vessel crossings of the macula have been described.

Specific Cone Dystrophies

CD Associated with GUCA1A

Onset is between the third and fifth decade with mild photophobia and reduced central vision. There is a generalized dyschromatopsia with no evidence of nystagmus. The mode of inheritance is AD. Ophthalmoscopy reveals a range of macular phenotypes, from mild RPE changes to frank macular atrophy with a normal peripheral retina. In full-field ERG, cone single-flash and flicker amplitudes are markedly subnormal, but there is minimal implicit time-shift (which is unusual in most CDs). There is usually no abnormality of the rod system, but forms of cone-rod dystrophy have been described. The gene GUCA1A encodes the phototransduction protein guanylate cyclase-activating protein-1 (GCAP1).

X-Linked CD

A genetically heterogeneous disorder has been mapped to loci on Xp21.1 (COD1, OMIM 304020) and Xq27 (COD2, OMIM 300085). COD1 maps to a region that harbors the RPGR gene, mutations in which account for more than 70% of patients with XL retinitis pigmentosa. The majority of these mutations reside in one purine-rich exon, ORF15, encoding 567 amino acids with a repetitive domain rich in glutamic acid residues. Two families with XLPCD linked to Xp21.1 (COD1) have been identified with two different mutations in ORF15 in RPGR. In both families clinical findings were typical of CD with photophobia, reduced central vision, progressive macular atrophy, and reduced cone ERGs with normal rod responses in affected males. However, they were unusual in having a late onset of reduced vision in the fifth decade.

Diagnosis

The diagnosis of cone dystrophy is confirmed by full-field electroretinogram (ERG), demonstrating generalized cone system dysfunction. Under light-adapted conditions, the photopic ERG responses to bright flash and flickering bright stimulus with a frequency of 30 cycles per second (Hz) stimulate the cone system. In cone dystrophies, the photopic ERG is severely abnormal to nonrecordable, while the dark adapted rod ERG is normal to subnormal. While the rod tracing might not have normal amplitude, it is well formed and usually stable over time. The cone ERG progressively worsens over time and may become nonrecordable.

Visual fields will show central scotomata, while the peripheral field is usually normal.

Psychophysical testing of color vision demonstrates color abnormalities. Because all three classes of cone photoreceptor are usually affected, the color vision defects seen are along all three color axes, not infrequently progressing to complete loss of color vision over time.

A recent study of 15 patients with cone dystrophy examined the morphological characteristics of the outer retina on spectral-domain optical coherence tomography (SD-OCT). Four out of 15 patients showed no definite structural changes

on OCT, while 11 out of 15 patients had symmetric changes in the outer retinal layers in both eyes. These changes were categorized into (1) irregular foveal loss of the ellipsoid portion of the photoreceptor inner segment (ISe) band and obscurity of the border between the ISe band and the external limiting membrane (ELM), (2) central retinal thinning and segmental foveal loss of the ISe band, and (3) central foveal thickening of the ISe band and irregular perifoveal loss of the ISe band. The outer segment (OS) contact cylinder layer was not discernible and the RPE layer was thickened in all 11 patients.

Differential Diagnosis

Stationary congenital cone dysfunction syndromes – mainly achromatopsia (rod monochromatism) and blue cone monochromatism. These are usually characterized by absence of photopic cone responses in ERG and usually do not progress.

Cone-rod dystrophies involve the rod system as well, but to a lesser degree than the cone system.

Prophylaxis

Prenatal diagnosis can be performed in families in which the responsible gene has been identified.

Therapy

There is currently no specific treatment for CDs.

Patients' management includes correction of refractive errors and wearing of tinted lenses to ease symptoms of glare and low visual aids.

Prognosis

Cone dysfunction usually progresses over time. The rate of progression shows wide variability in the different families, but visual acuity usually deteriorates over time to the level of 6/60 or counting fingers.

A recent longitudinal, multicenter study examined 98 consecutive probands with cone dystrophy. Average duration of follow-up was 19 years. The mean age onset for CD was 16 years (standard deviation, 11). Ten years after diagnosis, 35% of patients had a bull's eye maculopathy, and 37% developed rod involvement on ERG. The mean age of legal blindness was 48 (standard error, 3.1) years.

Epidemiology

Cone dystrophy (CD) and cone-rod dystrophy (CRD) are the most common hereditary cone disorders with a frequency of 1:30,000–40,000 worldwide.

Cross-References

- ▶ Achromatopsia (Rod Monochromatism), Gene Defects Causing
- ▶ Blue Cone Monochromatism
- ▶ Cone-Rod Dystrophy
- ▶ Day Blindness (Hemeralopia), in Cone Dystrophies

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Cone-Rod Degeneration

► Cone-Rod Dystrophy

Cone-Rod Dystrophy

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Synonyms

Cone-rod degeneration

Definition

The cone-rod dystrophies are a heterogeneous group of inherited progressive retinal degenerative disorders, characterized by the primary progressive loss of cone photoreceptor function, with later or sometimes concomitant loss of rod photoreceptor function. Electroretinography (ERG) demonstrates generalized cone system dysfunction with milder rod system involvement.

There is considerable overlap between progressive cone (CD) and cone-rod dystrophies (CRDs), since cone dystrophies usually present in childhood or early adult life, with many patients developing rod photoreceptor involvement in later life.

Symptoms resemble those of CD, and include reduced visual acuity, color vision abnormalities and photophobia, but are followed later by night blindness due to rod involvement. Visual fields show a relative central scotoma with variable loss of peripheral fields.

Etiology

CRDs are most frequently non-syndromic, but they may also be part of several syndromes, such as Bardet-Biedl syndrome and spinocerebellar ataxia type 7 (SCA7).

Non-syndromic CRDs are genetically heterogeneous, inherited by autosomal dominant (AD), autosomal recessive (AR), or X-linked recessive (XL) inheritance. Most cases of progressive CD and CRDs are sporadic and probably represent autosomal recessive inheritance, but some may represent new AD mutations and, in severely affected males, XL disease.

Autosomal dominant cone-rod or cone dystrophy identified and mapped genes are AIPL1, CRX, GUCA1A, GUCY2D, PITPNM3, PROM1, PRPH2, RIMS1, SEMA4A, and UNC119, while mapped loci, still unidentified, are CORD4, CORD17, and RCD1.

Autosomal recessive cone-rod or cone dystrophy identified and mapped genes are ABCA4, ADAM9, C21orf2, C8orf37, CACNA2D4, CDHR1, CERKL, CNGA3, CNGB3, CNNM4, KCNV2, PDE6C, PDE6H, RAB28, RAX2, RDH5, RPGRIP1, and TTLL5, with an unidentified locus CORD8.

X-linked cone-rod or cone dystrophy identified and mapped genes are CACNA1F and RPGR, with an unidentified locus COD2.

The four major causative genes involved in the pathogenesis of CRDs are *ABCA4* (which causes Stargardt disease and also 30–60% of autosomal recessive CRDs), *CRX* and *GUCY2D* (which cause autosomal dominant CRDs), and *RPGR* (which causes about two-thirds of X-linked retinitis pigmentosa (RP) and also an undetermined percentage of X-linked CRDs). ABCA4 seems to be the most prominent causal gene of CRD, but a large proportion of AR-CRD cases are still with an unknown etiology.

The genes involved in CRD can be classified in four categories. The first category includes genes mostly responsible for CRDs cases. A predominant gene encodes the homeobox protein CRX, which controls rod and cone photoreceptor cell differentiation and survival. Most *CRX* mutations cause AD- CRD, with a prevalence estimated at 5–10% of dominant CRDs. The severity of the disease is highly variable, from mild to very severe cases. There are a few reports of dominant Leber congenital amaurosis (LCA) caused by *CRX* mutations, a condition which is usually recessive, as well as a few RP cases.

The second category includes genes mostly found in macular dystrophies, mainly the *ABCA4*, which is involved in the retinoid metabolism and causes the Stargardt disease. Mutations in the *ABCA4* gene are responsible for 30–60% of the cases with autosomal recessive CRDs. In some cases, the disease begins as a Stargardt macular dystrophy phenotype, which soon extends to the periphery. In other cases, the disease starts as a diffuse retinopathy with predominance of macular involvement. The *ABCA4* mutations linked to CRDs are truncating mutations, often on both alleles, whereas amino acid change mutations are more frequently found in Stargardt disease. Belonging to this second category, mutations of *GUCA1A* have been described in autosomal dominant CRD as well as in cone dystrophies. The *GUCA1A* gene encodes a protein that activates the guanylate cyclase (GC).

The third category includes two genes mostly found in RP cases. The RDS (PRPH2) gene encodes the outer segment protein peripherin/RDS. RDS mutations are involved in autosomal dominant RP, dominant CRD, and dominant macular dystrophy. CRDs due to mutations in the *RDS* gene are relatively moderate in comparison with autosomal recessive CRDs. The second gene codes for RPGR, which is involved in opsin trafficking. *RPGR* is the major causative gene for X-linked RPs, but it also accounts for some X-linked CRD with its locus referred as *COD1* or *CORDX1* and cone dystrophies. As for RPs, CRDs caused by mutations in the *RPGR* gene are severe and diagnosed early in life.

The 4th category includes genes found in LCA. CRD families with mutations in the *RPGRIP1* gene (AR inheritance) and *AIPL1* (AD) have been described. There are also several CRD families reported with mutations in *GUCY2D*, which is the major causative gene for LCA. In contrast to LCA patients, CRD patients with *GUCY2D* mutations have a dominant condition, the mutations being restricted to exon 13 encoding the dimerization domain of the guanylate cyclase.

Findings

The clinical signs of CRDs reflect the predominant involvement of cones, leading to decreased visual acuity and loss of sensitivity in the central visual field. Decrease in the visual acuity is the earliest symptom, with early photophobia and frequent dyschromatopsia, while evidence of rod involvement with associated night blindness occurs later. This fits the original description of the CRD entity in which cone loss precedes rod degeneration. However, in some cases, diffuse retinopathy affects simultaneously cones and rods, resulting in both night blindness and loss of visual acuity.

CRDs present first as a macular disease or as a diffuse retinopathy with predominance of the macular involvement. Typically, the age of clinical onset in humans is in the first decade of life or early adulthood, but milder cases are not recognized until later in life.

Fundus examination shows macular atrophy or a bull's-eye maculopathy in the early stages. Peripheral RPE atrophy, retinal pigmentation in the periphery and macula, arteriolar attenuation, and optic disc pallor can be seen in the late stages. The dark choroid sign may be seen on fluorescein angiography. A tapetal-like sheen that may change in appearance on dark adaptation (Mizuo-Nakamura phenomenon) has been described in association with X-linked CRD.

Diagnosis

Clinical diagnosis is based on the early decrease of visual acuity and photophobia, fundus findings,

subnormal photopic and scotopic ERG responses with predominant cone involvement, and progressive worsening of these signs.

The photopic ERG responses to bright flash and flickering bright stimulus are severely reduced and delayed, in keeping with generalized cone dysfunction. The dark-adapted (DA) ERG shows subnormal rod response to dim light and subnormal amplitudes of a and b waves to stronger flashes. There is predominant involvement of photopic (cones) over scotopic (rods) responses. The cone and rod ERG progressively worsens over time and may become nonrecordable.

Visual fields: a central scotoma appears first, followed by a variable degree of peripheral involvement.

Psychophysical testing of color vision demonstrates color abnormalities.

Spectral domain optical coherence tomography (SD-OCT) can be used to evaluate the retinal morphological changes in CRDs. A normal outer retina structure includes four bands in SD-OCT: the inner most band is the external limiting membrane (ELM), the second is the ellipsoid zone (EZ) of the inner segments, the third is the interdigitation zone (IZ) between the outer segments and the apical processes of the RPE, and the fourth is the RPE complex. A recent study described the outer retina structure in 24 eyes of 12 patients with CRD. SD-OCT scans demonstrated complete absence of the interdigitation zone in the entire length of SD-OCT scan in all 24 study eyes. Outside the foveal area, the external limiting membrane and ellipsoid zone were intact in all study eyes. The intensity of the ellipsoid zone was decreased in the entire length of SD-OCT scan in all study eyes. Within the foveal area, there was loss of the external limiting membrane and ellipsoid zone in 20 (83%) and 22 eyes (92%), respectively. The retinal pigment epithelium complex was identified in all study eyes.

Cone Dystrophy with Supernormal Rod Electroretinogram

It is a recessively inherited disorder, which was first reported by Gouras et al. in 1983. It is related to mutations in KCNV2, which encodes a subunit of a voltage-gated potassium channel expressed in both rod and cone photoreceptors.

Patients typically present in the first two decades of life with reduced visual acuity, photophobia, and color vision abnormalities, with some experiencing nyctalopia. Most patients are myopic. The fundus appearance may be normal in the early stages, but later there may be pigmentary disturbance at the macula and macular atrophy. Rings of parafoveal hyperautofluorescence can develop with age, and in older individuals, it may surround central areas of atrophy. Spectral domain optical coherence tomography characteristics are variable; disruption of photoreceptor inner-outer segment junction, optical gap at the foveola, and central retinal thinning are variably observed. The ERGs in cone dystrophy with supernormal rod ERG are diagnostic. The light-adapted ERGs are reduced and delayed, as in other cone dystrophies. The dark-adapted (DA) ERG has no detectable response to a very dim white, and to a stronger ISCEV standard dim flash (DA 0.01), the ERG shows extraordinary delay and is usually of subnormal amplitude. There is then a disproportionate increase in b-wave amplitude with relatively small increases in stimulus intensity. The DA 11.0 ERG has a normal a-wave slope and a broadened "squared" shape often with a late negative "peak" to the a-wave, which appears pathognomonic of the disorder when combined with the large increase in b-wave amplitude after relative small increase in stimulus intensity from the DA 0.01 ERG.

Differential Diagnosis

Cone dystrophies – CRD can be distinguished from CD by the early involvement of rod photoreceptors.

The main clinical signs in CD are loss of visual acuity, photophobia, dyschromatopsia, and cone involvement at ERG. However, in some cone dystrophies, there may be some rod involvement, particularly in late stage. In contrast to CRDs, rods remain at least partly spared at these late stages, whereas they are usually nonrecordable in late-stage CRD.

Rod-cone dystrophies, retinitis pigmentosa – A disease history characterized by predominant night blindness with prominent rod involvement on ERG. In RP rod function is lost faster than cone function, versus CRD, in which the rate of cone and rod loss is similar.

Maculopathies – in Stargardt disease, some advanced cases will show peripheral retinal involvement with cone-rod dysfunction in ERG.

Prophylaxis

Prenatal diagnosis can be performed in families in which the responsible gene has been identified.

Therapy

There is currently no specific treatment.

Patients' management includes correction of refractive errors, wearing of tinted lenses to ease symptoms of glare, and low visual aids.

Prognosis

The clinical course of CRDs is generally more severe and rapid than that of rod-cone dystrophies, leading to earlier legal blindness and disability. Patients are often severely visually disabled or legally blind by the end of the second decade of life.

A recent longitudinal, multicenter study examined 83 consecutive probands with CRD. Average duration of follow-up was 19 years. The mean age onset for CRD was 12 years (standard deviation, 11). Ten years after diagnosis, 51% of CRD patients had a bull's-eye maculopathy, and 70% showed absolute peripheral visual field defects. The mean age of legal blindness was 35 (standard error, 1.1) years.

Epidemiology

Estimated prevalence 1/40,000

Cross-References

- ▶ Atypical Retinitis Pigmentosa (RP)
- ▶ Cone Dystrophies/Degeneration
- ▶ Day Blindness (Hemeralopia), in Cone Dystrophies
- ▶ Stargardt Disease

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Confocal Fluorescence Microscopy

▶ Confocal Microscopy

Confocal In Vivo Microscopy

▶ Confocal Microscopy

Confocal Microscope

▶ Scanning Confocal Microscope

Confocal Microscopy

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Synonyms

Subtypes: Confocal fluorescence microscopy; Confocal in vivo microscopy

Definition

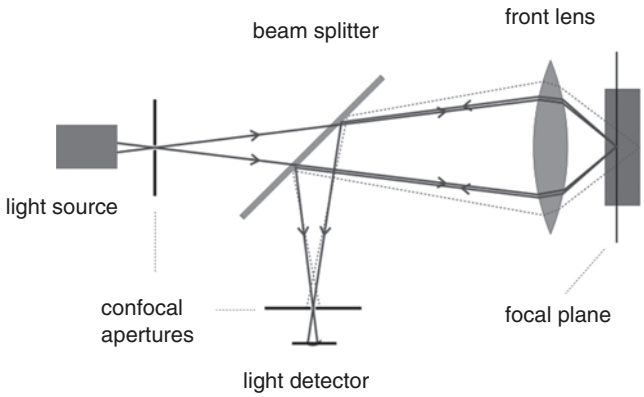
Method for imaging tissue (e.g., the cornea) on a cellular level with high resolution and magnification (ca. 200-fold). In contrast to optical coherence tomography, confocal microscopy produces optical sections in the frontal plane. In ophthalmology, confocal microscopy is used for both imaging tissue in vivo and ex vivo.

Purpose

Confocal microscopy is used to image the living cornea, conjunctiva, and sclera on a cellular level. Ex vivo virtually every type of tissue can be imaged with confocal fluorescence microscopy.

Principle

The principle of confocal imaging was described and patented by Marvin Minsky and aims to overcome the limitations of conventional wide-field microscopes. In a conventional microscope (e.g., light microscope or slit lamp), the entire tissue sample is flooded evenly in light. All parts of the specimen in the optical path reflect the light at the same time, and stray light scattered back from these out-of-focus layers blurs the in-focus image. In contrast, a confocal microscope uses a focused illumination (point or slit) and a pinhole in an optically conjugate plane in front of the detector to eliminate the out-of-focus light – hence the name "confocal" (Fig. 1). Because of the steep light gradient with maximum in the focal plane and the confocal pinhole, resolution is much better than that of conventional microscopes. Only details in the focal plane are imaged. As only one point (or slit) in the sample is illuminated at a time, imaging requires scanning over a raster in the specimen. The achievable thickness of the focal plane is defined mostly by the wavelength of the used light divided by the numerical aperture of the objective lens, but also by the optical properties of the specimen. For use in ophthalmology, two types of confocal in vivo microscopes are commercially available: A white-light slit-scanning microscope (ConfoScan, Nidek) and a laser scanning microscope (HRT RCM, Heidelberg Engineering) (Guthoff et al. 2006). There are numerous types of confocal



Confocal Microscopy, Fig. 1 The principle of confocal microscopy

fluorescence microscopes commercially available for examination of tissue samples ex vivo.

Indication

Confocal in vivo microscopy generates optical sections of the imaged tissue in the frontal plane similar to histological flat sections. The technique is particularly useful if conventional slit-lamp microscopy does not provide clear results, e.g., for differentiation of corneal opacities. One classical clinical indication is the search for trophozoites of *Acanthamoeba* spp. in case of keratitis (Winchester et al. 1995). With the laser scanning microscope, also the conjuctiva and sclera can be imaged. This can be helpful for the assessment of conjunctival neoplasias and filtering blebs after glaucoma surgery (Messmer et al. 2006a, b). Confocal in vivo microscopy is an important tool for monitoring corneal wound healing after corneal refractive laser surgery, particularly for scientific purposes.

Confocal fluorescence microscopy is an important technique in life sciences. In ophthalmology, this method is particularly useful for imaging corneal, retinal, and optic nerve tissue.

Contraindication

Confocal in vivo microscopy is a semi-invasive examination method, comparable to applanation or impression tonometry. Like in tonometry, there is potential danger of infection. If the cornea is applanated (HRT RCM), there can be mechanical irritation. The method must not be used in any case of open globe situation (e.g., injuries, early after intraocular surgery). Relative contraindications are keratitis and uncooperative, highly irritable patients. The cornea needs to be anesthetized with a local anesthetic. Therefore, allergy against local anesthetics is another contraindication.

Advantage/Disadvantage

Confocal in vivo microscopy provides unique information on a cellular level similar to histological sections far beyond magnification and resolution of the slit lamp. In some clinical cases, tissue biopsies can be avoided. In animal studies, intermediate results can be obtained during the time course without taking specimens. Because of their monochromatic nature, images obtained with the confocal in vivo microscope need a lot of experience to be interpreted. The technique is more invasive than a simple slit-lamp examination.

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Confocal Scanning Laser Ophthalmoscopy, in Retinal Examination

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Confocal Scanning Laser Ophthalmoscopy

Confocal scanning laser ophthalmoscopy (cSLO) is an ophthalmic imaging technology that scans an object point by point by a focused laser beam and then capturing the reflected light through a small aperture (a confocal pinhole). As opposed to conventional imaging technology which uses a bright flash of white light to

illuminate the retina, confocal technology requires the use of laser light instead of white light. The confocal pinhole, which is the core hallmark of the technology, suppresses light reflected or scattered from outside of the focal plane, which otherwise would blur the image. The result is a sharp, high-contrast image of the object layer located at the focal plane.

The advantages of using cSLO over traditional fundus photography include improved image quality as compare to standard photo, small depth of focus, and suppression of scattered light which eliminates image noise and patient comfort through less bright light. Because of the digital nature of the imaging process, 3D imaging capability and video capability are available. Due to the use of laser light which needs smaller capturing area, effective imaging is possible of patients who do not dilate well. This is especially valuable in diabetic patients, glaucoma patients and in elderly patients who typically do not dilate well. The cSLO also can penetrate hazy media as blood or opaque cataract due to the ability to increase the laser emission if needed.

Disadvantages of the use of cSLO imaging are the unnatural color images obtain as compare to white light. The cSLO scans the retina using several laser beams of different wavelength to produce color image and then superimpose the images obtain from each wavelength to construct a composite color image, but compare to the full spectrum of white light obtained from standard retinal photography and from clinical examination, the colors obtained look unnatural.

Congenital Anisocoria

▶ Physiologic Anisocoria

Congenital Color Vision Defects

▶ Inherited Color Vision Defects

Congenital Corneal Ectasia

▶ Staphylomas, Congenital, Anterior

Congenital Entropion

▶ Tarsal Kink

Congenital Gaze Palsy

▶ Congenital Ocular Motor Apraxia

Congenital Hereditary Endothelial Dystrophy

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Definition

Congenital hereditary endothelial dystrophy (CHED) is a rare corneal dystrophy characterized by bilateral, noninflammatory corneal clouding. There are two main forms of the disease, CHED 1 and CHED 2.

Etiology

CHED 1 is an autosomal dominant dystrophy with the gene locus on 20p11.2-q11.2.

CHED 2 is an autosomal recessive dystrophy with the gene locus on 20p13.

Clinical Presentation

In CHED 1, patients typically present within the first or second year of life with photophobia and tearing; then corneal clouding might follow. Corneal clouding might be asymmetrical and appears as a ground-glass milky appearance with significant corneal thickening. The photophobia and tearing seem to resolve by the time corneal clouding develops.

While in the CHED 2, the presentation is a diffused corneal coloring with a gray-blue ground-glass haziness of the corneal stroma within the first 6 months of age. Typically there is no or very slow progression; however, occasionally the corneal opacity might progress rapidly within the first year of life. Sometime stromal dots and flakes in deep cornea might be seen. Because of the severity of vision loss, some patients develop fine nystagmus.

Corneal thickness in CHED might be two to three times thicker than normal, with a central thickness more the 1 mm. The intraocular pressure and corneal diameters are normal which help in differentiating it from congenital glaucoma. The rest of the ocular structures are normal.

Diagnostics

There is no definitive diagnostic modality for CHED, which makes it a diagnosis of exclusion. However, when examination of a patient under general anesthesia shows the typical bilateral stromal opacification, gross corneal thickening, normal horizontal diameter, normal IOP, and the absence of brakes in Descemet's membrane, a provisional diagnosis of CHED can be made.

Histopathologically the corneal epithelium is thin or atrophic due to the corneal edema. Loss of Bowman's membrane is common and Descemet's membrane is usually thickened. The endothelial cells are either absent, reduced, or markedly degenerated.

Differential Diagnosis

Differential diagnosis includes congenital glaucoma, mucopolysaccharidosis, intrauterine infections (e.g., congenital rubella), birth trauma from forceps, and other corneal dystrophies (posterior polymorphous corneal dystrophy and macular stromal dystrophy).

Harboyan syndrome is an entity defined as CHED 2 and sensorineural hearing loss (perceptive deafness). This autosomal recessive disease is linked to the SLC4A11 gene mutation.

Prophylaxis

None. Genetic counseling might be helpful.

Therapy

Due to the involvement of the endothelium, full-thickness or endothelial keratoplasty is the mainstay of treatment.

Penetrating keratoplasty (PKP) in children is a complex surgery with multiple challenges like more risk of rejection and glaucoma than adult. One of the major limitations for vision improvement in this group of age is amblyopia. One study of PKP for CHED showed that around two thirds of eyes of patients who underwent PKP had clear graft at 2 years; however, the visual acuity improvement was limited with approximately two thirds of patients who had 20/400 visual acuity or, worse, poor vision in clear graft cases which was thought to be attributed to the development of amblyopia. Adding to the relatively poor results, penetrating keratoplasty in young children has risk of vision-threatening complication such as suprachoroidal hemorrhage.

Descemet stripping automated endothelial keratoplasty (DSAEK) is thought to be safer and has less risk of vision-threatening complications like suprachoroidal hemorrhage. However, DSAEK graft survival is still unclear in this group.

Prognosis

The prognosis is highly dependent on the age of onset. The success rate of corneal transplant

surgery at young age is less compared to older patients because of more risk of rejection and complication. Congenital-onset CHED has less graft survivability and success rate compared to "delayed-onset" CHED.

Epidemiology

It is a rare corneal dystrophy except in specific areas, like Saudi Arabia and South India.

Cross-References

- ▶ Posterior Polymorphous Corneal Dystrophy
- ▶ Primary Congenital Glaucoma

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Congenital Hereditary Endothelial Dystrophy (CHED)

- ▶ Corneal Dystrophies

Congenital Hereditary Stromal Dystrophy

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C

Synonyms

Congenital stromal dystrophy of the cornea

Definition

A congenital stromal corneal dystrophy characterized by central clouding of the cornea without edema and a clear peripheral cornea.

Etiology

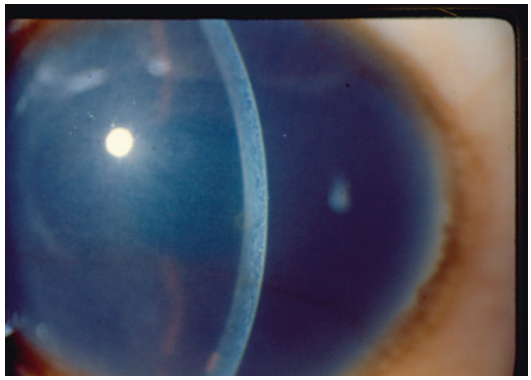
An autosomal dominant disease with a genetic mutation on chromosome 12 involving the Decorin-*DCN* gene (Krachmer et al. 2011).

Clinical Presentation

Patients present at birth with a bilateral clouding of the central cornea involving only the stroma (Rødahl et al. 1993–2013). The epithelium and endothelium are normal, and no erosions, vascularization, or edema are found. Closer examination reveals flake-like lesions in the anterior and posterior stroma and less prominent in the periphery (Weiss et al. 2008). Patients experience a moderate to severe loss of vision that progresses slowly or not at all. Dense amblyopia with a searching nystagmus may be seen in some patients (Fig. 1) (Krachmer et al. 2011).

Diagnostics

Diagnosis is made with clinical presentation and family history. Adjuncts are histology with transmission electron microscopy (TEM) and confocal



Congenital Hereditary Stromal Dystrophy, Fig. 1 Clouding of the central cornea without edema

microscopy. Histology demonstrates smaller than normal collagen fibrils with alternating layers of normal and randomly arranged fibrils. Some areas of the stromal lamellae have amorphous deposits. On TEM, the lamellar layers consist of randomly arranged filaments in an electron-lucent ground substance. Confocal microscopy demonstrates increased reflectivity in the anterior stroma (Weiss et al. 2008).

Differential Diagnosis

Differential diagnosis includes congenital glaucoma, corneal ulcer, interstitial keratitis, Peter's anomaly, congenital hereditary endothelial dystrophy, or metabolic abnormalities such as mucopolysaccharidoses and mucolipidoses.

Therapy

Depending on the degree of corneal cloudy and potential of dense amblyopia, penetrating keratoplasty may be performed at a young age. The corneal pathology does not recur in the donor graft (Krachmer et al. 2011).

Prognosis

Patients usually have moderate to severe vision loss. Even with intervention, visual acuity rarely improves beyond 20/200 (Krachmer et al. 2011).

Epidemiology

The prevalence of the disease is unknown other than it is rare.

Cross-References

- Congenital Hereditary Endothelial Dystrophy (CHED)
- Corneal Dystrophies
- Corneal Ulcers
- Interstitial Keratitis
- Primary Congenital Glaucoma

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Congenital Hypertrophy of Retinal Pigment Epithelium

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Solitary or multiple, discrete round or oval-shaped, flat, gray to black-pigmented lesions composed of hypertrophied retinal pigment epithelium, lined by degenerated photoreceptor layer. It is congenital, benign, and asymptomatic.

Common abbreviation for congenital hypertrophy of the retinal pigment epithelium is CHRPE. When lesions are multiple and grouped together, they are described as "bear tracks."

Congenital Ocular Melanocytosis

▶ Blue Nevus

Congenital Ocular Motor Apraxia

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Synonyms

Cogan's apraxia; Cogan type; COMA; Congenital gaze palsy; Congenital saccadic palsy; Ocular motor apraxia

Definition

Congenital ocular motor apraxia (COMA) is a rare congenital disorder of conjugate gaze characterized by a defect or absence in voluntary horizontal gaze, compensatory head thrusting, and often retention of both slow pursuit and reflexive eye movements (Olitsky et al. 2011).

Epidemiology

COMA is a very rare disorder and is more common in boys than in girls. It is estimated to occur in less than one in 1,000,000 members of the population (Lavin 2012).

History

COMA was first described in a case report published by Cogan in 1952 (Cogan 1952).

Clinical Features

By 4–8 months of age, the infant typically develops a thrusting head movement strategy, with prominent blinking, to overcome the eye movement deficit. Since the vestibulo-ocular reflex (VOR) prevents a change in direction of gaze on head rotating, the infant closes the eyes to reduce the degree of reflex eye movement while thrusting the head beyond the range of the VOR arc to bring the eyes in line with the target. Then, with the eyes open, the infant slowly straightens the head, while the contralateral VOR maintains fixation. Some patients may use the dynamic head thrust to facilitate saccadic eye movements or reflexively to induce fast phases of vestibular nystagmus (Lavin 2012). Because children with COMA cannot easily pursue new targets before they develop the head thrusting strategy, especially in early infancy, they are sometimes misdiagnosed as being blind (Lavin 2012). Most affected children have delayed motor and speech development including delayed sitting, clumsiness, and gait disturbances (Olitsky et al. 2011).

Tests

Magnetic resonance imaging (MRI) of the brain to rule out cerebral or cerebellar malformations. Test for ataxia-telangiectasia and lysosomal storage diseases, which are often associated with COMA.

Differential Diagnosis

Consider the possibility of ocular motor apraxia in any infant referred for evaluation of visual impairment. If the infant is at least 4 months of age, he or she may display the thrusting head movement strategy outlined in the clinical features section. Additionally, with the head held immobile, the child may not make an effort to initiate horizontal eye movements (Piña-Garza 2013). Studies have indicated a variety of anatomic abnormalities that can be seen on an MRI in children with congenital ocular motor apraxia, including inferior vermian hypoplasia, dysgenesis of the corpus callosum, cerebellar hypoplasia, and posterior fossa tumor (Sargent et al. 1997).

Etiology

COMA has been associated with multiple genetic deletions or mutations; however, more research needs to be done to identify specific genetic causes and hereditary patterns (Lavin 2012).

Treatment

There is no known cure or treatment for COMA. Patients typically benefit from supportive therapies like speech and language therapy, physiotherapy, and occupational therapy. Special education support has been reported to help children adapt to learning at school. As children reach school age, their symptoms variably improve. However, the condition typically does not completely resolve and can be detected in adulthood (Lavin 2012).

Cross-References

► Ocular Motor Apraxia

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Congenital Saccadic Palsy

► Congenital Ocular Motor Apraxia

Congenital Stromal Dystrophy of the Cornea

► Congenital Hereditary Stromal Dystrophy

Congenitally Anomalous Disk

► Pseudopapilledema

Conjunctiva

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Basic Characteristics

The conjunctiva is a transparent mucous membrane that lines the posterior surface of the eyelids and covers the globe and orbit. Its primary functions are to act as a physical anatomic barrier to

the environment, to allow for smooth movement of the eye, to help to maintain a suitable environment for the ocular surface and cornea, and also to play a role in immune protective mechanisms of the external eye. Abnormalities of the conjunctiva may lead to restriction of ocular motility, tear film deficiency, and decreased host resistance to infection.

The conjunctiva is embryologically derived from the surface ectoderm. The conjunctiva is divided into the palpebral, forniceal, and bulbar portions. The palpebral portion begins at the mucocutaneous junction of the eyelid and covers the inner surface of the eyelid; it is firmly adherent to the tarsal plate. The forniceal conjunctiva becomes redundant and freely movable. It continues as the bulbar conjunctiva where it fuses with the Tenon capsule and inserts into the corneoscleral limbus

The anterior ciliary arteries supply blood to the bulbar conjunctiva, and branches of the marginal arcades of the lids supply the palpebral and forniceal portions. The innervation is derived from the ophthalmic division of cranial nerve V.

The conjunctiva is the main site for the production of the aqueous and mucous components of the tears. It consists of nonkeratinized stratified squamous epithelium with mucin-secreting goblet cells overlying a loose layer of abundantly vascularised lamina propria. The goblet cells are concentrated in the inferior and medial portions and are sparsely distributed throughout the remainder of the conjunctiva.

Additionally, there is a lymphoid layer with specialized aggregations of conjunctiva-associated lymphoid tissue (CALT) which comprise collections of T and B lymphocytes that function in antigen processing.

Cross-References

- ▶ Conjunctival Autograft
- ▶ Conjunctival Degenerations
- ▶ Conjunctival Flaps
- ▶ Conjunctival Inclusion Cysts
- ▶ Conjunctival Melanoma
- ▶ Conjunctival Nevus
- ▶ Conjunctival Tumors
- ▶ Conjunctivitis
- ▶ Conjunctivochalasis
- ▶ Glands of Krause, Glands of Moll, Glands of Wolfring, Glands of Zeis
- ▶ Palpebral Conjunctiva
- ▶ Tear Film (Tears)

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Conjunctival Autograft

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Synonyms

Conjunctival autografting; Conjunctival autograft transplantation; Conjunctival free flap (misnomer); Free conjunctival autograft transplantation; Free conjunctival transplant

Definition

Conjunctival graft should be considered in comparison to conjunctival flap. In the graft technique, the tissue is harvested and transplanted to different

sites without any blood supply. On the other hand, a conjunctival flap has a remaining attachment to the origin site and carries its own blood vessels.

Indication

Common indications for conjunctival graft are:

- Pterygium (the most common indication)
- Cicatricial ocular surface disease (symblepharon)
- Conjunctival tumor lesions

Amniotic membrane is used as alternative of conjunctival graft in these indications.

Contraindication

Conjunctival autograft should not be prepared from a site with history of trauma or surgery. Eyes with uncontrolled inflammation and dry eye disease are not good candidates for conjunctival graft harvest. Amniotic membrane grafts should be considered in glaucoma patients to increase the chance of future successful trabeculectomy if needed. However, inferotemporal conjunctiva could be considered as a potential harvest site in these patients. Furthermore, combined nasal and temporal pterygium or large defects are difficult to be managed by conjunctival graft. The graft should not be transplanted to sites with ischemia, and instead, conjunctival flap should be considered.

Techniques and Principles

These factors are important for successful conjunctival autograft:

1. Obtain adequate size of graft (usually 1 mm oversize).
2. Harvest the graft without the Tenon's tissue and avoid buttonhole.
3. Securely fix the graft in the recipient site.

As superotemporal conjunctiva is mostly selected for graft harvest, tractional suture with Vicryl 6-0 or Silk 6-0 can be used for better exposure of the field. The defect site should be measured. It is recommended that the conjunctiva is outlined 1 mm larger than the defect size with gentian violet and pay attention not to connect harvest and recipient site with each other. Lidocaine with diluted adrenalin is subconjunctivally injected. It makes dissection easier between the conjunctiva and Tenon's layer. Dissection is started in lateral borders with blunt Westcott scissors. Anterior and posterior borders are cut later in order to maintain the conjunctiva in flat position, and conjunctiva dissection form Tenon's capsule can be done more easily in this condition. The surgeon should attempt not to leave the Tenon under the conjunctiva and avoid perforation of the graft. The conjunctiva should be gently grasped with fine instrument. The harvest site is left bare or covered with amniotic membrane. Caution should be taken about the orientation of the graft. If the graft is transplanted upside down, it will cause graft necrosis (Brightbill 2009; Krachmer et al. 2010; Copeland et al. 2013).

Conjunctival autograft can be fixed with sutures or fibrin glue. It is recommended that using nylon 10-0 instead of Vicryl 8-0 or 9-0- because nylon cause less inflammation and pterygium recurrence may be less than using Vicryl suture. The graft usually is sutured at the limbus and conjunctiva border with separated or running sutures. Although fibrin glue is more costly than suture, it will reduce surgical time and patients' discomfort. It is shown that fibrin glue reduces the recurrence of pterygium in comparison with sutures (Pan et al. 2011).

Outcome

Conjunctival autograft is the preferred procedure for pterygium surgery. The procedure is simple and can be done everywhere. The reported recurrences rates are usually under 10%. In comparison with amniotic membrane use in pterygium surgery, conjunctival graft surgery has less recurrence rate and better cosmetic result and is more affordable (Kaufman et al. 2013).

Complications

Possible complications that may occur include:

- Graft edema
- Graft hemorrhage
- Graft dislocation or loss
- Graft retraction
- Graft necrosis
- Corneoscleral dellen
- Infection
- Pyogenic granuloma in the recipient or harvest site
- Epithelial inclusion cysts

Cross-References

► Conjunctival Flaps
► Pterygium

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Conjunctival Autograft Transplantation

► Conjunctival Autograft

Conjunctival Autografting

► Conjunctival Autograft

Conjunctival Chalasis

► Conjunctivochalasis

Conjunctival Concretions

► Lithiasis, Conjunctival

Conjunctival Degenerations

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Synonyms

Concretions; Conjunctivochalasis; Pinguecula; Pterygium

Pinguecula

Pingueculae are nodules of bulbar conjunctival thickening that are typically paralimbal at 3 and 9 o'clock positions. Pingueculae may be unilateral or bilateral and are more commonly found nasally. The nodules consist of hyaline and collagen elastic tissue.

Etiology

Pingueculae are thought to be caused by actinic damage via ultraviolet radiation, which results in elastotic degeneration of the conjunctival substantia propria. It is unclear why nasal lesions are more common than temporal ones, although some have theorized that it may be due to the reflection of the sun off of the nose (Perkins 1985; Brodbaker et al. 2008). Other potential causes of pingueculae include trauma, foreign body agitation (e.g., dust), and drying.

Clinical Presentation

Pingueculae are elevated yellowish-white lesions that are located in the interpalpebral conjunctiva. They do not invade the cornea and have few, if any vessels. The lesion may become red and inflamed and the diagnosis of pingueculitis is then assigned Fig. 1.

Diagnosis

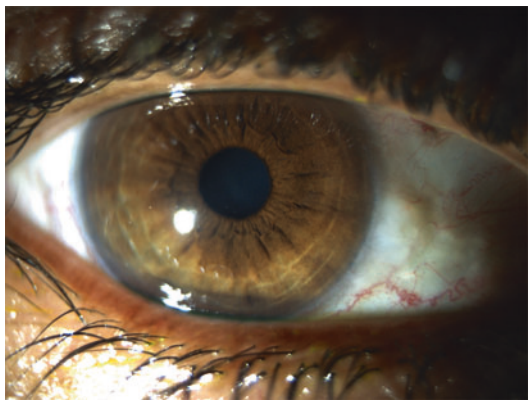
The diagnosis is based on clinical examination. In atypical cases, a tissue diagnosis may be obtained.

Differential Diagnosis

Pterygium
Bitot spot (vitamin A deficiency)
Phlyctenule
Episcleritis
Nodular scleritis
Conjunctival intraepithelial neoplasia
Squamous cell carcinoma
Conjunctival granuloma

Prophylaxis

UV protection with the use of wide brimmed hats and UV-protecting sunglasses can be helpful in preventing the occurrence of pingueculae. Protection from chronic wind and dust exposure minimizes the potential ocular surface irritation that can lead to pingueculae formation.



Conjunctival Degenerations, Fig. 1 Pinguecula (Note the yellowish-white mound located nasal to the limbus)

Therapy

Treatment is often not indicated. Artificial tears can be used for lubrication. A short-term course of a topical vasoconstrictor and/or topical steroid may be indicated for pingueculitis. Surgical excision may be indicated for inflamed lesions unresponsive to conservative management.

Prognosis

Pingueculae are benign lesions with no immediate sight-threatening implications, although they can sometimes cause contact lens intolerance. Pingueculae are associated with a two- to threefold increased incidence of age-related macular degeneration, possibly through a common light exposure effect (Pham et al. 2005). Pingueculae that are tan in color may be associated with Gaucher's disease type I (Chu et al. 1984).

Epidemiology

The prevalence varies among populations, but pingueculae are more prominent in more heavily pigmented populations and in people over 40 years of age.

Pterygium

A pterygium is a slowly progressive, degenerative, fibrovascular, and fleshy winglike growth extending from the conjunctiva unto the cornea.

Etiology

Pterygia are associated with ultraviolet light exposure, dust, drying, and windy environments.

Clinical Presentation

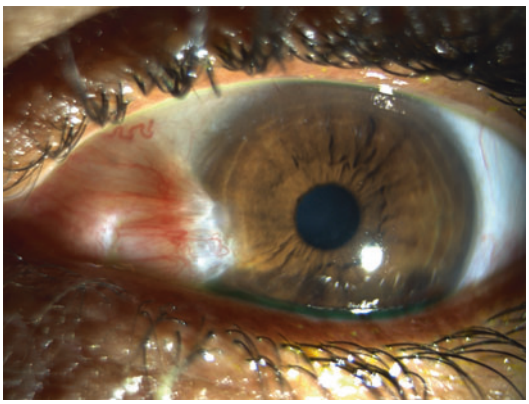
Pterygia are often nasal and bilateral but they can also occur temporally. They can induce astigmatism and, if central enough, can obstruct the visual axis. Patients with pterygia may present with a redness, irritation, foreign body sensation, photophobia, contact lens intolerance, and/or cosmetic concerns regarding the lesion(s) (Kaufman et al. 2013; Young et al. 2013). Whitish opacities, named Islets of Vogt, can be found on the surface of many pterygia, and a linear deposit of iron may be seen on the cornea at the leading edge of the pterygium, called a Stocker line. Pterygia may be exacerbated by keratoconjunctivitis sicca or via trauma (Fig. 2).

Diagnosis

The diagnosis is based on clinical examination. Confirmatory evidence can be obtained via tissue diagnosis following a biopsy or a surgical removal procedure.

Differential Diagnosis

- Cyst
- Phlyctenule
- Episcleritis, scleritis
- Ocular cicatricial pemphigoid



Conjunctival Degenerations, Fig 2 Pterygium (Note the fleshy, fibrovascular, and winglike growth extending from the conjunctiva past the limbus onto the cornea)

- Resolved marginal keratitis
- Squamous cell carcinoma
- Conjunctival intraepithelial neoplasia
- Focal limbal stem cell deficiency
- Hereditary benign intraepithelial neoplasia
- Mucoepidermoid carcinoma
- Pseudoepitheliomatous hyperplasia

Prophylaxis

UV protection with the use of wide brimmed hats and UV-protecting sunglasses can be helpful in preventing the occurrence of pterygia (Mackenzie et al. 1992). Also, protection from chronic wind and dust exposure minimizes the potential ocular surface irritation that can lead to pterygium formation (Mackenzie et al. 1992).

Therapy

Treatment is often not indicated. Artificial tears can be used for lubrication. A short-term course of a topical vasoconstrictor and/or topical steroid may be indicated for an inflamed pterygium. Surgical excision is warranted for recurrent or chronically inflamed lesions, astigmatism, direct involvement of the visual axis, contact lens intolerance, and in cases of significant cosmetic concern (Kaufman et al. 2013). Surgical technique varies from simple excision to procedures associated with lower recurrence rates such as conjunctival and amniotic membrane grafts. Fibrin glue can be used as an aid to tack down the conjunctival grafts. Mitomycin C, β-irradiation, and thiotepa have also been used to lower the rate of recurrence, each with its own set of risks (Young et al. 2013).

Prognosis

Most pterygia are asymptomatic or mild symptomatic and symptom relief can often be obtained using artificial tears. Pterygia have a high recurrence rate after simple excision alone. Recurrences are reduced by the use of conjunctival autograft, β-irradiation, thiotepa, or mitomycin C in the treatment process. Surgical excision of

recurrent pterygia is significantly more complex, owing to copious scar tissue. There is a very small malignant potential, and pterygia specimens are usually submitted for review.

Epidemiology

Pterygia are more common in males than females, particularly among those who live closer to the equator and who work outdoors. The lesions tend to be more prominent in more heavily pigmented populations and in people between 20 and 40 years of age (Perkins 1985).

Concretions

Concretions are chalky-white-to-yellow keratin and epithelial debris-containing cysts located in the fornix or inferior or superior palpebral conjunctiva.

Etiology

Concretions are associated with increasing age and chronic inflammation which causes invagination of conjunctival epithelial cells. Erosion through the overlying conjunctiva can cause a foreign body sensation. Concretions may be secondary, as in the late stages of trachoma.

Clinical Presentation

Concretions are often incidental findings but can occasionally cause a foreign body sensation.

Diagnosis

The diagnosis is based on clinical examination.

Differential Diagnosis

Inclusion cyst
Follicles
Foreign body
Granuloma
Conjunctival tumor
Buildup of meibum

Prognosis

Concretions are typically benign, producing no symptoms. If bothersome, they often respond well to simple excision.

Epidemiology

Concretions occur at a higher incidence with increasing age or chronic inflammation. In a sample taken in the United Kingdom, concretions were found in over 40% of patients, the vast majority of whom were asymptomatic (Kulshrestha and Thaller 1995).

Conjunctivochalasis

Conjunctivochalasis refers to a redundancy of the bulbar conjunctiva between the globe and lower eyelid margins.

Etiology

The etiology is poorly understood and still being researched. It is theorized that it may be due to blockage of lymphatic flow causing lymphatic dilation and eventual conjunctival elastosis and redundancy.

Clinical Presentation

Patients vary in the degree of their symptomatology ranging from being asymptomatic to experiencing ocular irritation, pain, subconjunctival hemorrhage, epiphora, dry eye, and/or ulceration. The symptoms are often exacerbated by blinking.

Diagnosis

Slit lamp examination shows a redundant fold of conjunctiva over the sclera that is usually more pronounced with downgaze and improved with upgaze.

Differential Diagnosis

Chemosis
Acute or chronic conjunctivitis
Dry eye
Conjunctival tumors

Prognosis

Mildly symptomatic patients are often treated with artificial tears, lubricating gels, corticosteroid or antihistamine drops, and/or nocturnal patching as a first line of treatment. Surgery can be performed to remove the redundant conjunctiva with employment of amniotic membrane grafting with sutures and/or and fibrin glue.

Epidemiology

Conjunctivochalasis occurs at an increased rate in the elderly.

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Conjunctival Edema

▶ Chemosis

Conjunctival Epithelial Inclusion Cyst

▶ Conjunctival Inclusion Cysts

Conjunctival Epithelial Melanosis

▶ Melanosis

Conjunctival Epithelial Tumor

▶ Dacryoadenoma

Conjunctival Flaps

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Definition

A surgical procedure that entails advancing or rotating a conjunctival pedicle into an adjacent defect.

Indication

Conjunctival flaps have a broad variety of applications. Gunderson flaps have long been used for eyes with poor visual potential and exposure, neurotrophic ulcers, band keratopathy, advanced bullous keratopathy, or the need to comfortably fit a cosmetic scleral shell. More recently, rotational flaps have been proposed as an alternative to

conjunctival autografts in pterygium surgery. They are also used to treat tube erosion with glaucoma drainage devices (Godfrey et al. 2003).

Contraindication

Gunderson flaps in particular are difficult to perform in eyes with multiple prior surgeries and/or scarring due to absence of mobile conjunctiva. Conjunctival flaps to cover glaucoma drainage tubes should not be used if the flap design would incorporate tissue directly adjacent to the lacrimal gland ductules.

Techniques and Principles

Gunderson flaps are created by making liberal conjunctival incisions in the superior and inferior fornices. The conjunctiva is then separated from underlying Tenon's capsule and a 360° peritomy is performed. This creates two flaps that can be advanced over the cornea and sutured together. The corneal epithelium must be thoroughly debrided prior to flap closure (Maguire and Shearer 1991).

Conjunctival flaps for pterygium surgery are designed similarly to autographs, but a limbal anchoring point approximately 1 mm wide is preserved to act as a vascularized pedicle (Kim et al. 2013). The flap is then rotated into the bare scleral defect and sutured.

Flaps to cover eroded glaucoma drainage implants are created such that the length to width ratio is approximately 3:1 (Grover et al. 2013). Tissue is generally recruited from the conjunctival fornix, and the base of the pedicle is created adjacent to, but not on, the drainage plate. Lid splitting can be performed for better visualization and access if needed. The eroded tube is first covered with a new corneal or preserved scleral patch graft and then the rotational flap.

Outcome

The Gunderson flap is generally very successful in reducing ocular surface discomfort (Ma'luf and Awwad 2005). Several authors have reported that rotational flaps for pterygium surgery offer equivalent success rates to autografts with decreased edema and reduced operating time. Pedicle flaps for tube erosion are effective compared to other techniques, but up to half of complex cases still may require additional repairs.

Complications

Complications include dehiscence, retraction, pterygium recurrence, and recurrent corneal or tube exposure.

Cross-References

- ▶ Bulla
- ▶ Conjunctival Autograft
- ▶ Conjunctiva
- ▶ Pterygium

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Conjunctival Free Flap (Misnomer)

- ▶ Conjunctival Autograft

Conjunctival Hemorrhage

▶ Subconjunctival Hemorrhage

Conjunctival Inclusion Cysts

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Synonyms

Conjunctival epithelial inclusion cyst; Inclusion cyst of conjunctival epithelium

Definition

Benign, cystic lesion of conjunctiva derived from an inclusion of conjunctival epithelium into the substantia propria (American Academy of Ophthalmology (nd); Shields and Shields 2008).

Etiology

Congenital or more commonly acquired due to chronic inflammation, trauma, or surgery. Inclusion of epithelium into the substantia propria leads to epithelial cell proliferation with resultant formation of a central cavity lined by nonkeratinized conjunctival epithelium (American Academy of Ophthalmology (nd); Shields and Shields 2008).

Occurrence

Uncertain but acquired lesions are commonly seen (American Academy of Ophthalmology (nd); Shields and Shields 2008).

Classification

Congenital or acquired.

Cross-References

▶ Conjunctiva
▶ Conjunctival Melanoma
▶ Conjunctival Tumors
▶ Conjunctival Papilloma

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Conjunctival Inflammation

▶ Conjunctivitis

Conjunctival Injection

▶ Hyperemia, Conjunctival

Conjunctival Intraepithelial Neoplasia (CIN)

▶ Carcinoma In Situ, of Conjunctiva
▶ Squamous Dysplasia of Conjunctiva

Conjunctival Lithiasis

▶ Concretions, Conjunctival

Conjunctival Melanoma

▶ Pigmented Lesions of the Conjunctiva

Conjunctival Melanosis

▶ Melanosis

Conjunctival Nevus

▶ Pigmented Lesions of the Conjunctiva

Conjunctival Papilloma

▶ Human Papilloma Viruses, Ocular Infection

Conjunctival Squamous Cell Carcinoma

▶ Squamous Cell Carcinoma, of the Conjunctiva

Conjunctival Squamous Cell Papilloma

▶ Papillomas, Conjunctival

Conjunctival Squamous Dysplasia

▶ Carcinoma In Situ, of Conjunctiva
▶ Squamous Dysplasia of Conjunctiva

Conjunctival Tumor

▶ Epibulbar Tumor

Conjunctival Tumors

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Definition

Conjunctival tumors are a large and varied spectrum of disorders ranging from benign to malignant lesions.

Basic Characteristics

The majority of conjunctiva tumors are benign and malignant tumors and are relatively rare. Conjunctival epithelial tumor is more common than stromal tumor. The former one can be classified according to the type of cells. In general, there are three basic categories of conjunctival tumors including the ones arising from the squamous epithelium, associated with melanocytes, or lymphoid cells.

1. Squamous epithelial lesions:
   - Squamous papillomas
   - Ocular surface squamous neoplasia
2. Melanocytic tumors:
   - Nevus
   - Primary acquired melanosis
   - Melanoma
3. Glandular tumor:
   - Oncocytoma
4. Lymphocytic lesions:
   - Benign lymphoid hyperplasia
   - Lymphoma
5. Other neoplasms: Tumor may occasionally arise in the conjunctiva, including neural, muscular, vascular, and fibrous tumors and metastatic lesions.

Further Reading

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Conjunctival Xerosis

▶ Xerosis

Conjunctivitis

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Synonyms

Conjunctival inflammation; Madras eye; Pink eye

Definition

Conjunctivitis refers to inflammation of the conjunctiva, the outer lining of the ocular surface and posterior eyelids, and is generally characterized by vascular dilation causing a hyperemic appearance. Additional features or involvement of additional ocular layers vary based on etiology.

Etiology

The etiology of conjunctivitis is broadly categorized into acute and chronic causes.

Acute conjunctivitis	
Categories	Common agents
Infectious: Bacterial	*Neisseria gonorrhoeae*, *Neisseria meningitidis, Staphylococcus aureus*, *Streptococcus pneumoniae*
Infectious: Viral	Adenoviruses types 3 and 7 causing pharyngoconjunctival fever, Adenoviruses types 8 and 19 causing epidemic keratoconjunctivitis, Herpes simplex virus, Varicella-zoster virus, Epstein-Barr virus, Cytomegalovirus
Infectious: Fungal	*Candida albicans*
Chemical	Preservatives in eye drops and contact lens solutions, idoxuridine, brimonidine, apraclonidine, dipivefrin
Traumatic	
Chronic conjunctivitis	
Infectious: Bacterial	*Chlamydia, S. aureus*, *Moraxella lacunata*, *Actinomyces israelii*
Infectious: Viral	Adenoviruses types 2, 3, 4, and 5. Molluscum contagiosum virus
Infectious: Other	*Sporothrix schenckii, Rhinosporidium seeberi, Coccidioides immitis, Thelazia californiensis, Loa loa, Ascaris lumbricoides, Trichinella spiralis, Schistosoma haematobium, Taenia solium, Pthirus pubis*
Unknown etiology	Chronic follicular conjunctivitis, psoriasis, folliculosis

Conjunctivitis can also be categorized as bacterial or viral in origin. There are many other causes of conjunctivitis that include, chlamydial, fungal, parasitic, rickettsial, allergic, chemical (irritative), associated with systemic diseases like tuberculosis or syphilis, secondary to dacryocystitis or canaliculitis, or unknown in etiology.

Bacterial conjunctivitis		
Type	Duration of illness	Common agents
Hyperacute	Few hours to 3 days	*Neisseria gonorrhoeae*, *Neisseria meningitidis*
Acute	21 days	*Staphylococcus aureus*, *Streptococcus pneumoniae.* Less common*: C. diphtheria*, *S. epidermidis*, *Pseudomonal* species, *Escherichia coli*, *Shigella* species, *Borrelia vincentii*, *Fusobacterium bacilli*
Chronic	Long term (more than 3 weeks)	*Chlamydia, S. aureus*, *Moraxella lacunata*, *Actinomyces israelii* (most common canalicular pathogen)

Bacterial conjunctivitis can be classified into hyperacute, acute, and chronic based on the duration of illness. Hyperacute conjunctivitis is most commonly caused by *Neisseria gonorrhoeae* and *Neisseria meningitides. N. gonorrhoeae* is the most common pathogen causing hyperacute bacterial conjunctivitis (Krachmer et al. 2011).

Staphylococcus aureus and *Streptococcus pneumoniae* are common causes of acute bacterial

conjunctivitis. *H. influenza* (nonencapsulated) is the most common cause of bacterial conjunctivitis in children. *C. diphtheriae* and *S. epidermidis* are infrequent causes of acute bacterial conjunctivitis. Other bacteria are *Pseudomonal* species, *Escherichia coli*, *Shigella* species, *Borrelia vincentii*, and *Fusobacterium bacilli* among others.

Chronic bacterial conjunctivitis is most commonly caused by *S. aureus*. *Moraxella lacunata* is also a common cause. *Actinomyces israelii* is the most common canalicular pathogen. *Chlamydia* can cause chronic inclusion conjunctivitis and also trachoma.

Viral conjunctivitis is most commonly caused by adenoviruses, accounting from 65% to 90% of all viral etiologies. Other causes of viral conjunctivitis are Herpes simplex virus, Varicella-zoster virus, Epstein-Barr virus, Cytomegalovirus, Variola (smallpox) virus, Vaccinia (cowpox) virus, Molluscum contagiosum virus, Picornaviruses (enterovirus and coxsackievirus), Paramyxoviruses (measles, mumps, and Newcastle disease), Rubella (German measles), and Flaviviruses (yellow fever and dengue).

Clinical Presentation

Bacterial Conjunctivitis

Bacterial conjunctivitis is usually bilateral and is characterized by a purulent or mucopurulent discharge. In **hyperacute bacterial conjunctivitis** there is marked conjunctival hyperemia, lid edema, chemosis, and copious amounts of purulent discharge (Krachmer et al. 2011). There may be membranes or pseudomembranes which are associated with preauricular adenopathy. It usually starts unilaterally and often becomes bilateral and the incubation period is anywhere from a few hours to 3 days. In ophthalmia neonatorum caused by *N. gonorrhoeae*, there is chemosis 2–4 days after transit through an infected birth canal along with a hyperacute purulent conjunctivitis.

Acute bacterial conjunctivitis is arbitrarily defined as having a duration of less than 3 weeks. It is also less severe than hyperacute bacterial conjunctivitis. The discharge is mucopurulent but may be mucoid (catarrhal) or purulent. There is frequently a velvety papillary reaction seen on the palpebral conjunctivae. *S. aureus* is associated with a characteristic blepharitis and the mucopurulent discharge may lead to stickiness of the eyelids in the morning. The incubation period for *S. pneumoniae* is about 2 days and maximum severity is reached in 2–3 days after onset. Subjunctival hemorrhages are frequently seen and usually involve the upper tarsal conjunctiva or fornix (Krachmer et al. 2011).

Chronic bacterial conjunctivitis is characterized by symptoms that last longer than 3 weeks and has a more indolent course. Symptoms can be variable but include minimal discharge, foreign body sensation, and stickiness and matting of the eyelashes. Clinical signs include diffuse conjunctival hyperemia, papillae formation, and a mild mucopurulent discharge (Krachmer et al. 2011). *S. aureus* can cause blepharoconjunctivitis with concurrent lid margin involvement with loss of lashes, trichiasis, hordeola, telangiectasis, and erythema (Krachmer et al. 2011). *M. lacunata* causes a follicular conjunctivitis. *Actinomyces* can cause unilateral itching, tearing, and irritation. Mucopurulent drainage can be seen from the puncta and milking of the canaliculi can yield yellow granular material from the punctum (sulfur granules).

Chlamydia conjunctivitis is typically found in young adults and is sexually transmitted. There may be a history of urethritis, cervicitis, or vaginitis. It causes a stringy mucous discharge along with follicles on the inferior tarsal and bulbar conjunctiva, peripheral SEIs, and superior corneal pannus. There is also palpable preauricular lymphadenopathy. Trachoma occurs primarily in endemic areas such as India, Southeast Asia, North Africa, and the Middle East, in areas of overcrowding and poor sanitation. According to the WHO classification, the TF phase (trachomatous inflammation: follicular) presents with five or more follicles on the upper tarsus. The TI phase (trachomatous inflammation: intense) includes inflammation with thickening obscuring >50% of the tarsal vessels. The TS phase (trachomatous scarring) is characterized by

cicatrization of tarsal conjunctiva with fibrous white bands. The TT phase (trachomatous trichiasis) includes trichiasis of atleast one eyelash and the CO phase (corneal opacity) involves corneal opacity involving at least part of the papillary margin.

Viral Conjunctivitis

Viral conjunctivitis is characterized by conjunctival hyperemia, tearing, gritty, or foreign body sensation, sticking of the eyelids or crusting (worse in the mornings), and less than 4 weeks of symptoms. The onset is acute after about 5–14 days. The discharge is watery, and the eyelids are red and edematous. There is a follicular reaction of the conjunctiva and pinpoint subconjunctival hemorrhages can be seen. Superficial punctuate keratopathy, membrane/pseudomembrane, and subepithelial infiltrates can develop as well. It typically starts in one eye and involves the fellow eye a few days later. It is spread by personal contact, swimming pools, or through fomites. **Pharyngoconjunctival fever** is characterized by pharyngitis, fever, preauricular and cervical adenitis, and follicular conjunctivitis. It can also be accompanied by diarrhea and rhinitis (Krachmer et al. 2011). **Epidemic keratoconjunctivitis** is more severe than pharyngoconjunctival fever but there is an absence of extraocular manifestations with severe stromal infiltrates. There can be worsening of photophobia, tearing, and discomfort which signifies keratitis. The keratitis can be superficial but can progress to subepithelial infiltrates. Pseudomembranes and membranes signify severe conjunctival involvement. **Acute nonspecific follicular conjunctivitis** is characterized by milder conjunctival involvement and keratitis that is limited to the epithelium if at all. There is a mild follicular reaction, mild conjunctival hyperemia, and discrete lid edema (Krachmer et al. 2011).

Chronic viral conjunctivitis is characterized by symptoms that can last for months or even years. There are intermittent symptoms including irritation with waxing and waning superficial punctate keratitis and subepithelial infiltrates. **Herpes simplex conjunctivitis** usually presents with unilateral disease with a follicular reaction, mucous drainage, conjunctival hyperemia, and preauricular lymphadenopathy. Dendritic keratitis may be present initially or develop later. Superficial punctuate keratitis can be present without dendritic lesions. **Varicella-zoster virus** can rarely cause conjunctivitis. Phlyctenule-like lesions that are small and ulcerative are found at the limbus, and the cornea can also be affected. The reactivation of varicella in the trigeminal ganglion involves the V1 dermatome and is called **herpes zoster ophthalmicus. Epstein-Barr virus (EBV)** presents with fever, sore throat, lymphadenopathy, lymphocytosis, polyarthritis, myositis, and follicular conjunctivitis (Krachmer et al. 2011). **Cytomegalovirus (CMV)** can also present with follicular conjunctivitis. **Variola and Vaccinia conjunctivitis** are rare. They present with pustules on bulbar conjunctivae along with purulent discharge. **Molluscum contagiosum virus (MC)** typically presents with a follicular conjunctivitis, corneal pannus along with lid margin lesions. These lesions are umbilicated, dome shaped, raised, and flesh colored. Enterovirus and coxsackieviruses can cause **acute hemorrhagic conjunctivitis (AHC)**. This syndrome begins with acute onset of pain, lacrimation, FB sensation, conjunctival injection, subconjunctival hemorrhages along with periorbital swelling (Krachmer et al. 2011). AHC may resemble EKC, but AHC has a more rapid disease course and has less corneal involvement than EKC. The **paramyxoviruses (measles, Newcastle disease, and mumps)** are characterized by follicular conjunctivitis. In measles, catarrhal conjunctivitis, superficial keratitis, and photophobia are the most common clinical features (Krachmer et al. 2011). Keratitis can be severe and can cause blindness. In Newcastle disease, mild follicular conjunctivitis along with subepithelial infiltrates might be seen. In mumps, the parotid salivary glands get swollen. If the lacrimal gland is affected, then there can be orbital pain and a mass. Superficial punctuate keratitis or stromal keratitis may be seen. **Rubella** is a mild childhood disease and presents with follicular conjunctivitis and punctuate keratitis located in the central cornea. **Yellow fever and dengue fever** are arthropod-borne illnesses common in the tropics.

They are characterized by conjunctival injection, lid edema, and photophobia. Conjunctival hemorrhages can be seen if coagulopathy develops (Krachmer et al. 2011).

Diagnosis

Bacterial Conjunctivitis

In cases of hyperacute bacterial conjunctivitis, gram staining and confirmatory culture are mandatory for diagnosis because of the possibility of systemic infection and bacterial resistance.

Acute bacterial conjunctivitis is diagnosed by clinical signs and symptoms and without laboratory studies. Lab studies should be obtained in acute conjunctivitis refractory to treatment and severe conjunctivitis in infants and children (Krachmer et al. 2011).

Diagnosis of chronic bacterial conjunctivitis is often made by history and clinical exam findings; however, culturing of the lid margin and conjunctiva is important in refractory cases. In chronic follicular conjunctivitis, Gram and Giemsa staining may reveal *Moraxella* or *Chlamydia*. Direct *chlamydial* immunofluorescence test, DNA probe, *chlamydial* culture of conjunctiva, or PCR is used to diagnose *chlamydial* conjunctivitis.

Viral Conjunctivitis

Viral conjunctivitis is clinically diagnosed based on acute conjunctivitis, follicles on the inferior tarsal conjunctiva, preauricular lymphadenopathy, a recent URI, and contact with a person who had red eye. If symptoms persist or the condition is chronic, then cell culture along with confirmatory immunofluorescence staining can be obtained. HSV conjunctivitis can be diagnosed clinically; however, the gold standard method for diagnosis is cell culture. Varicella-zoster conjunctivitis is diagnosed clinically but cell cultures can be sent. EBV is diagnosed clinically as is CMV conjunctivitis. Variola and vaccinia conjunctivitis are diagnosed clinically but viral studies can be obtained if the diagnosis is in doubt. MC conjunctivitis is diagnosed by history and clinical exam. Diagnosis of AHC is based on clinical findings but cultures and PCR can be used to isolate the offending pathogen. Conjunctivitis from paramyxoviruses is diagnosed clinically. Togavirus and Flavivirus conjunctivitis are also diagnosed clinically.

Differential Diagnosis

Various conditions present with the appearance of an inflamed conjunctiva, not all of which are infectious. In addition to directly infectious etiologies, which may be bacterial, viral, fungal, or parasitic, the differential of an injected conjunctiva includes:

Immune modulated

- Allergic conjunctivitis
- Vernal keratoconjunctivitis
- Atopic keratoconjunctivitis
- Superior limbic keratoconjunctivitis
- Giant papillary conjunctivitis (often secondary to contact lens wear)
- Inflammation from adjacent structures (e.g., dacrocystitis and canaliculitis)
- Blepharoconjunctivitis
- Keratoconjunctivitis sicca

Trauma

- Floppy eyelid syndrome
- Mucous fishing syndrome
- Toxic papillary keratoconjunctivitis
- Chemical conjunctivitis
- Subconjunctival hemorrhage

Vacsular

- Ligneous conjunctivitis (deficiency in fibrinolysis)
- Lymphangioma (focal reddening may be associated with subconjunctival hemorrhage in a "chocolate cyst" formation)

Neoplastic

- Lymphoma (fleshy, salmon colored in appearance)

Prophylaxis

Prophylaxis is mandatory for contacts of patients with *N. meningitidis* conjunctivitis because of the risk of contracting or carrying the disease. This is accomplished by Rifampin 600 mg PO twice daily for 2 days for adults and a dose of 10 mg/kg for children.

Patients with acute viral conjunctivitis thought to be adenoviral in origin should be instructed in proper hygiene in order to avoid transmission to close contacts, as well as to avoid cross-contamination to the contralateral eye in unilateral cases.

Therapy

Hyperacute Conjunctivitis

N. meningitidis conjunctivitis is treated with 300,000 IU/Kg per day of penicillin administered IV or IM. Topical penicillin G 100,000 IU/mL per hour can also be prescribed. Gonococcal conjunctivitis is treated with a single IM dose of 1 g ceftriaxone followed by a one-time saline lavage of the conjunctiva. A single dose of 1 g of oral azithromycin or 100 mg of oral doxycycline twice a day for 7 days should also be given to treat concomitant chlamydial infection and reduce the risk of post-gonococcal urethritis and salpingitis (Krachmer et al. 2011). *N. gonorrhoeae* conjunctivitis in the newborn is treated with 25–50 mg/kg of IV or IM ceftriaxone administered in a single dose (not to exceed 125 mg) along with concurrent saline irrigation of the conjunctiva.

Acute Bacterial Conjunctivitis

Topical antibiotic therapy with broad spectrum antibiotic ointments or eye drops like trimethoprim/polymyxin B or fluoroquinolone drops q.i.d. for 5–7 days is given for acute bacterial conjunctivitis. *H. influenza* conjunctivitis is treated with oral amoxicillin/clavulanate (20–40 mg/kg/day in three divided doses) since it can be complicated by otitis media, meningitis, and pneumonia.

Chronic Bacterial Conjunctivitis

Chronic *staphylococcal* conjunctivitis often involves the lids, requiring long-term therapy. This includes lid hygiene, lid margin cleansing with mild baby shampoo diluted 50% with water, and the nightly application of bacitracin to the lid margins (good Gram+ coverage). For *chlamydial* conjunctivitis, azithromycin 1 g PO as a single dose, doxycycline 100 mg PO b.i.d., or erythromycin 500 mg PO, q.i.d., for 7 days is given to the patient and sexual partners. Topical erythromycin or tetracycline ointment b.i.d to t.i.d. for 2–3 weeks can also be prescribed. For trachoma, azithromycin 20 mg/kg PO single dose, doxycycline 100 mg PO b.i.d., erythromycin 500 mg PO q.i.d., or tetracycline 250 mg PO q.i.d. for 2 weeks is adequate (Gerstenblith and Rabinowitz 2012).

Viral Conjunctivitis

Viral conjunctivitis treatment and prevention involve avoiding touching the eyes, shaking hands, or sharing towels or pillows. Patients should frequently wash their hands. Single tip vials of preservative-free artificial tears four to eight times per day for 1–3 weeks can be used along with cool compresses several times a day. If there is itching, then epinastine 0.05% b.i.d. can be used as well. If membranes/pseudomembranes are present, then loteprednol 0.5% q.i.d. can be used, although for subepithelial infiltrates, a lower concentration of loteprednol 0.2% b.i.d. is often sufficient.

HSV conjunctivitis must be treated in neonates with both topical and intravenous acyclovir. In adults, treatment is mandatory when dendritic corneal lesions are present. 3% vidarabine or 3% acyclovir ointment for 10–14 days is prescribed. Oral acyclovir may also be given. VZV can be treated with ganciclovir 0.15% or vidarabine 3% ointment t.i.d. or q.i.d. EBV and CMV conjunctivitis are treated symptomatically. Vaccinia conjunctivitis is treated with ganciclovir 0.15% ophthalmic gel five times a day for 2 weeks. Vaccinia immune globulin 100 mg/kg IM or 6,000 units/kg IV is also given.

Molluscum contagiosum conjunctivitis lesions may be treated by unroofing and curettage,

although alternative therapies such as excision and cryotherapy have been utilized. Acute hemorrhagic conjunctivitis is treated symptomatically with cold compresses and artificial tears. For measles, Newcastle disease, and mumps conjunctivitis, no specific treatment is available. Rubella is treated with topical lubricants, while flavivirus conjunctivitis is treated symptomatically.

Prognosis

Hyperacute and acute bacterial conjunctivitis is almost always self limited. If properly treated, it lasts 1–3 days and if untreated it may last 10–14 days (Riordan-Eva and Cunningham 2011). *Staphylococcal* conjunctivitis is an exception as it may progress to blepharoconjunctivitis and enter a chronic phase. *Neisseria* infections can cause serious corneal damage. There can be rapid development of corneal haze and peripheral infiltrates followed by ulcerations of the cornea leading to corneal perforation. Patients with *N. meningitides* conjunctivitis are also at risk of developing meningitis and other systemic manifestations like septicemia.

Phlyctenular keratoconjunctvitis, corneal opacities, and marginal corneal ulceration may develop after *H. influenzae*, biogroup *aegyptius* conjunctivitis. URI, fever, malaise, otitis media, and meningitis may also be caused by *H. influenzae*.

S. aureus can cause a number of corneal complications including corneal epithelial punctate erosions and punctate keratitis. Marginal corneal infiltrates and ulcerations can frequently be seen near the limbus at the 4 and 8' o clock positions. Phlyctenules may also be seen (Krachmer et al. 2011).

Trachoma can lead to trichiasis and subsequent corneal scarring and opacity if untreated.

Viral conjunctivitis is a self-limited conjunctivitis and is worse in the first 4–7 days and usually resolves in 4 weeks. HSV conjunctivitis usually resolved within 2 weeks even without treatment. Ocular vaccinia is usually self limiting. MC conjunctivitis often resolves in 4–6 weeks. AHC is self limiting. In measles conjunctivitis, resolution of symptoms is seen in 3–5 days. Newcastle disease conjunctivitis resolves without sequelae in 7–10 days. Togavirus and flavivirus conjunctivitis are self limiting.

Epidemiology

The global burden of conjunctivitis is seen most strongly with trachoma, from which 8 million people are visually impaired and an estimated 84 million people with active disease require treatment to prevent blindness.

Cross-References

- ▶ Acute Hemorrhagic Conjunctivitis
- ▶ Adenoviral Keratoconjunctivitis
- ▶ Allergic Conjunctivitis
- ▶ Blepharoconjunctivitis
- ▶ Canaliculitis
- ▶ Chemical Injury (Burns)
- ▶ Conjunctivochalasis
- ▶ Follicular Conjunctivitis
- ▶ Giant Papillary (Contact Lens-Induced) Conjunctivitis Disease
- ▶ Gonococcal Conjunctivitis
- ▶ *Haemophilus influenzae*, Conjunctivitis
- ▶ Herpes Zoster Ophthalmicus
- ▶ Hyperemia, Conjunctival
- ▶ Ligneous Conjunctivitis
- ▶ Limbal Vernal Conjunctivitis/Keratoconjunctivitis
- ▶ Palpebral Vernal Conjunctivitis/Keratoconjunctivitis
- ▶ Pseudomembrane, Conjunctival
- ▶ Syphilis: Overview
- ▶ Vernal Conjunctivitis/Keratoconjunctivitis

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Conjunctivochalasis

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Synonyms

Conjunctival chalasis

Definition

Conjunctivochalasis (CCh) is a Greek term for "relaxation of conjunctiva" and was first described by Braunschweig on 1921 (Hughes 1942). It is an isolated condition that tends to be bilateral, and it is characterized by redundancy and laxity of the conjunctiva which typically affects the inferior bulbar conjunctiva, located between the globe and the lower eyelid (Liu 1986; Meller and Tseng 1998).

Etiology

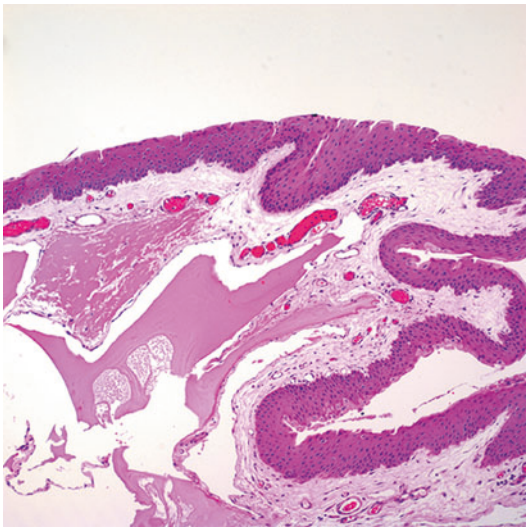
While the pathophysiology has not been entirely established, it has been often considered as a variation of normal aging and as a result of mechanical forces between the lower eyelid and the conjunctiva due to increased pressure of the lower lid margin. This continuous stimulus interferes with the lymphatic flow which, when chronic, may result in lymphatic dilatation and eventually, conjunctivochalasis (American Academy of Ophthalmology 2012) (Fig. 1).

Clinical Presentation

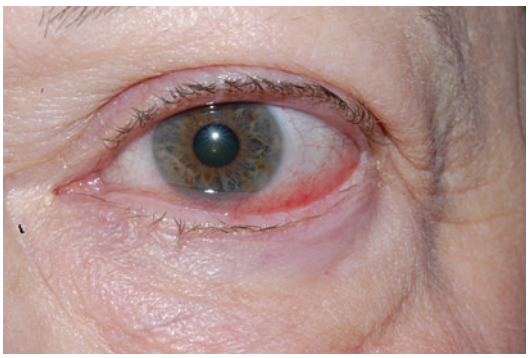
In general, this condition is asymptomatic. However, various clinical problems may present ranging from exacerbation of dry eye at mild stage due to impaired moisture of the extra conjunctival tissue, to tearing secondary to normal tear outflow disruption at the moderate stage, to interference with the inferior tear meniscus, and, less frequently, to occlusion of the lower punctum when this redundant conjunctiva is prominent medially. Subconjunctival hemorrhage might be present in patients with chronic inflamed fragile tissue or secondary to mechanical rubbing. Foreign body sensation and irritation can also be present.

Diagnosis

CCh diagnosis is based on clinical findings during slit-lamp examination and does not require



Conjunctivochalasis, Fig. 1 Conjunctivochalasis, left eye (should be the clinical photo)



Conjunctivochalasis, Fig. 2 Histologic findings in conjunctivochalasis; subepithelial lymphoplasmocytic infiltrate, Hematoxylin & Eosin, 40X

expensive equipment for further testing. In general, CCh lacks inflammatory signs, and fluorescein or rose Bengal staining tends to be negative. Nevertheless, chronic exposure of this loose conjunctiva may result in discrete or punctate staining in addition to localized mild chronic inflammatory changes seen on the redundant tissue, particularly, in the bulbar and tarsal conjunctiva (Fig. 2). Previous authors (Höh et al.) (Table 1) have suggested an objective and reliable system for grading CCh according to the number of folds and height of redundant conjunctiva in relation to the tear meniscus. However, these parameters may vary with age and downgaze. As a result, Meller and Tseng proposed a new grading system which includes the extension of CCh and gaze-dependent changes (Table 2). In this modified system, digital pressure is also considered as a factor in estimating the extent of severity since some patients due to previous surgeries may develop increased pressure and worsen CCh. However, no consensus in the diagnostic criteria has been established and remains subject of debate.

Conjunctivochalasis, Table 1 Grading of conjunctivochalasis by LIPCOF[a]

Grade	Number of folds and relationship to the tear meniscus height
0	No persistent fold
1	Single, small fold
2	More than two folds and not higher than the tear meniscus
3	Multiple folds and higher than the tear meniscus

[a]Modified from Höh et al.[7] with permission of the authors and ophthalmologe

Differential Diagnosis

CCh can be easily mistaken with other ophthalmological entities that also present with tearing and foreign body sensation such as allergy, keratoconjunctivitis sicca (KCS), trichiasis, ectropion, punctum stenosis, or any nasolacrimal obstruction. Systemic conditions including thyroid eye

Conjunctivochalasis, Table 2 Proposed new grading system for conjunctivochalasis[a]

Location	Folds versus tear meniscus height	Punctal occlusion	Changes in downgaze	Changes by gigital pressure
0	A	O+	G⇑	P⇑
1	B	O−	G⇔	P⇔
2	C		G⇓	P⇓
3				
0: none	A: < tear meniscus	O+ = nasal location with punctal occlusion	G⇑ = height/extent of chalasis increases in downgaze	P⇑ = height/extent of chalasis increases on digital pressure
1: one location	B: = tear meniscus			
2: two locations	C: > tear meniscus			
3: whole lid		O− = nasal location without punctal occlusion	G⇔ = no difference G⇓ = height/extent of chalasis decreases in downgaze	P⇔ = no difference P⇓ = height/extent of chalasis decreases on digital pressure

[a]The new grading system defines the extension of redundant conjunctiva as grade 1 = one location, 2 = 2 locations, 3 = whole lid. For 1 and 2, it is further specified as T, M, and N if conjunctivochalasis is found in the temporal, the middle (or inferior to the limbus), and the nasal aspect of the lower lid, respectively. For each location (T, M, and N), further notation is given to indicate if the height of folds is less than (A), equal to (B), or greater than (C) the tear meniscus height. If it is found in the nasal (N) location, the extent of chalasis is further determined as to whether it occludes the inferior puncta. For each location, it is further graded as G⇑ if its height is greater than, as G⇔ if equal to, and as G⇓ if less than the tear meniscus height. Likewise it is further graded as P⇑, P⇓, and P⇑ if it is worse, no difference, or better with digital pressure (P), respectively

disease, allergy, and dry eye including aqueous tear deficiency (ATD) can also present with similar symptoms.

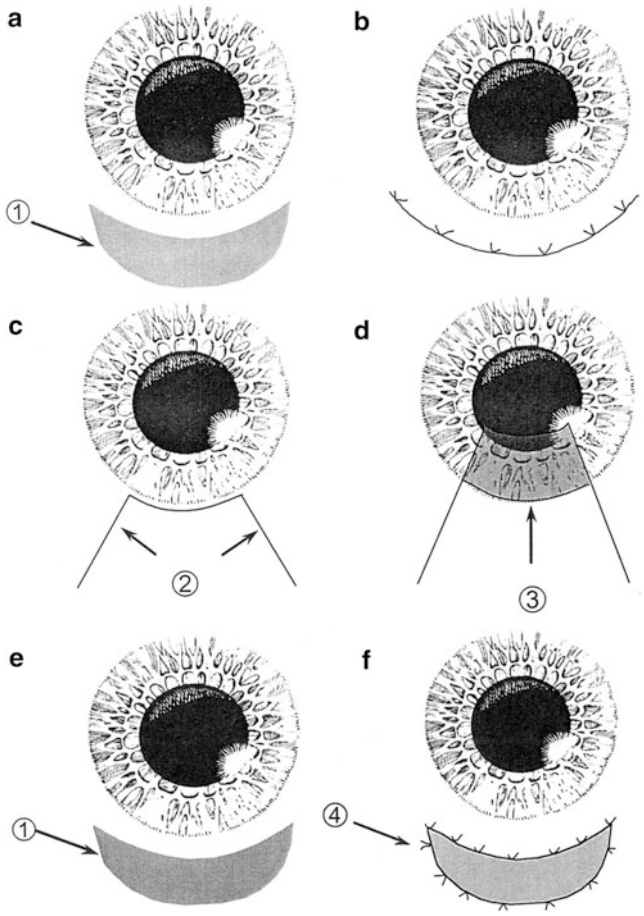
Prophylaxis

Since this condition is often related to aging and block of lymphatic flow, no specific alternatives to prevent it have been described.

Therapy

Asymptomatic CCh does not require treatment. Medical therapy with topical lubricants, anti-inflammatory, and antihistamines may be offered as treatment options for symptom relief. Night patching may be used when symptoms are more severe. When none of the above is effective regardless of patient compliance, surgical treatment becomes a definitive therapy. Surgical excisions of that loose conjunctiva or having it fixed to the sclera are current available approaches. Furthermore, cauterizations of the redundant tissue folds and amniotic membrane grafts have also been offered as treatment.

A variety of surgical techniques to excise the redundant conjunctiva have been described; the most commonly used is a simple crescent excision of the inferior redundant bulbar conjunctiva 5 mm away from the limbus (marked as 1 in Fig. 3a, e) and subsequent closure with absorbable sutures (Fig. 3b). Other authors have proposed a modified technique which includes a peritomy made close to the limbus (marked as 2 in Fig. 3c) as well as



Conjunctivochalasis, Fig. 3 Surgical excision techniques of redundant conjunctiva

two radial relaxing incisions to excise the redundant conjunctiva (marked as 3 in Fig. 3d). A recent modification to the above techniques to reduce the frequency of complications after surgery has been proposed. The use of amniotic membrane graft to replace the affected surface after conjunctival excision has been described (marked as 4 in Fig. 3f) (Meller and Tseng 1998).

Surgeons must be aware to perform careful excision and avoid aggressive resection regarding the technique to reduce rate of complications such as visible scarring, cicatricial entropion, and retraction of the lower fornix that may result in motility restriction and/or corneal problems. Other postsurgical findings including scar formation, suture-induced granulomas, and inflammation surrounding the amniotic graft have also been associated.

Prognosis

CCh is a benign condition that has an excellent prognosis.

Epidemiology

CCh is equally seen in men and women; it is well known to be a degenerative age-related condition and is most commonly seen in the elderly population.

Cross-References

► Conjunctival Degenerations

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Connective Tissue Disease

► Connective Tissue Disorder of the Cornea

Connective Tissue Disorder of the Cornea

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Synonyms

Connective tissue disease

Definition

Connective tissue disorders refer to a family of more than 200 disorders that affect the biologic tissue that connects, binds, supports, or separates different types of tissues and organs in the body. These disorders can either be heritable, which is due to mutations in the genes responsible for the structure and development of these tissues, or they can be autoimmune, which is due to overactivity of the immune system resulting in the production of antibodies that attack the body's own tissues. Both hereditary and autoimmune connective tissue disorders can affect virtually every site in the body, including the skin, bones, blood vessels, heart, lungs, gastrointestinal tract, kidneys, and eyes (Long et al. 2013). More specifically within the eyes, connective tissue disorders have marked effects on the structure and function of the cornea. Ehlers-Danlos syndrome (EDS) type VI and Marfan syndrome are two common hereditary connective tissue disorders affecting the cornea, while numerous autoimmune connective tissue disorders do so as well, including rheumatoid arthritis, systemic lupus erythematosus (SLE), Behçet's disease, Sjogren's disease, scleroderma, granulomatosis with polyangitis, polyarteritis nodosa, and relapsing polychondritis (Wisenthal et al. 2013).

Etiology

Connective tissues contain three principle components: (1) fibroblasts or their counterpart in the cornea, the keratinocyte, (2) ground substance, and (3) fibrous elements comprised of the protein molecules elastin and collagen. Elastin is encoded by the ELN gene, is formed by cross-linked amino acids, and allows many tissues in the body to return to their original shape after stretching. Collagen, on the other hand, is encoded by 34 genes and consists of a triple helix of three amino acid chains. There are four types of collagen found in the body, and each differs from the other by their molecular composition. Type I is present in the corneal stroma, skin, bone, and tendon, type II in the cartilage, type III in the fetal skin and blood vessels, and type IV in basement membranes (Maumenee 1978).

Hereditary connective tissue disorders are transmitted in a simple Mendelian manner and have generalized defects in either collagen or elastin. Ehlers-Danlos syndrome is composed of more than 20 different types of disease, though EDS type VI, known as the ocular-scoliotic type, is the primary one affecting the cornea. It is inherited in an autosomal recessive manner and is secondary to a mutation in locus 1p36 (PLOD1), the gene-encoding lysyl hydroxylase, the enzyme necessary for the formation and stabilization of collagen. Marfan syndrome is inherited in an autosomal dominant manner and is caused by a mutation in locus 15q21.1 (FBN1), the gene-encoding fibrillin-1, a protein essential for the proper formation and maintenance of elastic fibers, including elastin (Kanski and Bowling 2011; Wisenthal et al. 2013).

Autoimmune connective tissue disorders may have both environmentally induced and genetically predisposing causes. As a group, they are characterized by an overactive immune system, one that produces antibodies directed against one's own tissues. These autoantibodies may directly target sites in the corneal epithelium, and they may also result in immune complex deposition in the peripheral cornea, which then recruits further inflammatory cells that release matrix metalloproteinases that degrade collagen and the extracellular matrix (Kanski and Bowling 2011).

Clinical Presentation

Ehlers-Danlos syndrome type VI is associated with many systemic changes, including the thin and hyperelastic skin that bruises easily, hypermobile joints, scoliosis, dissecting aneurysms, and diverticula of the gastrointestinal and respiratory tract in addition to ocular pathology including thinned blue sclera that may rupture easily and epicanthal folds. There are also several abnormalities specific to the cornea, such as microcornea, keratoconus, keratoglobus, and a brittle structure that may easily rupture with trauma (Kanski and Bowling 2011; Wisenthal et al. 2013). Marfan syndrome is also associated with many specific systemic features, including thin, tall stature with disproportionately long limbs, pectus carinatum or excavatum, arachnodactyly, kyphoscoliosis, high-arched palate, dilation of the aortic root, aortic aneurysm, and mitral valve prolapse, in addition to ocular features such as ectopia lens with superotemporal subluxation, cataracts, retinal detachment associated with lattice degeneration, hypoplasia of the dilator pupillae, strabismus, and glaucoma secondary to angle dysgenesis. Marfan syndrome too has many cornea-specific changes, including megalocornea, keratoconus, and cornea plana with excessive flattening in the 35 diopter range of the corneal curvature (Kanski and Bowling 2011; Wisenthal et al. 2013), or more than three standard deviations below normal values of the US population (Maumenee 1978).

Autoimmune connective tissue disorders manifest in the cornea as peripheral ulcerative keratitis (PUK). This occurs most commonly with rheumatoid arthritis but also systemic lupus erythematosus (SLE,) Behçet's disease, Sjogren's disease, scleroderma, granulomatosis with polyangitis, polyarteritis nodosa, relapsing polychondritis, and several more. While these conditions have many varied systemic presentations, PUK may be the first sign of an underlying systemic disease or may indicate exacerbations of systemic disease activity (Wisenthal et al. 2013). PUK usually presents unilaterally and limited to one area of the peripheral cornea; however, it may also be bilateral and extensive. The lesions, which

are characterized by a crescenteric area of absent epithelium and thinned underling stroma, appear within two millimeters of the limbus and are associated with vaso-occlusion of the adjacent limbal vasculature. They may also have significant cellular infiltrate into the corneal stroma as well as adjacent limbitis, episcleritis, or scleritis. In advanced cases, corneal perforation may occur (Kanski and Bowling 2011).

Diagnosis

Ehlers-Danlos syndrome can be diagnosed by the Beighton criteria, which use physical exam to assess the degree of joint hypermobility. Additionally, genetic testing for mutations in collagen genes, skin biopsies to evaluate hydroxylysine levels, and urine studies to detect an abnormal ratio of lysyl pyridinoline to hydroxylysyl pyridinoline may be used to confirm the diagnosis (Long et al. 2013; Wisenthal et al. 2013). The diagnosis of Marfan syndrome is made using the Ghent criteria, which require the detection of major and minor criteria in three body systems by physical exam and imaging or the detection of fibrillin-1 mutation by genetic testing (Long et al. 2013). Corneal manifestations of the ectasias seen in both Ehlers-Danlos type VI and Marfan syndrome may be found with slit lamp microscopy, keratometry, anterior segment ultrasound, and B-scan ocular ultrasound (Kanski and Bowling 2011; Wisenthal et al. 2013). The peripheral ulcerative keratitis seen in autoimmune connective tissue disorders may be diagnosed with slit lamp microscopy. Additionally, though not a standard diagnostic procedure, biopsy of conjunctival tissue adjacent to the corneal disease would show immune-mediated vaso-occlusive changes (Wisenthal et al. 2013).

Prophylaxis

There is no known prevention of the corneal dysgeneses seen in the heritable forms of connective tissue disorders, namely, Ehlers-Danlos and Marfan syndrome. However, control of underlying systemic disease with immunosuppression may play a role in preventing the peripheral ulcerative keratitis associated with autoimmune connective tissue diseases (Kanski and Bowling 2011; Wisenthal et al. 2013).

Therapy

Errors of refraction commonly arise from the abnormal corneal curvature seen in Ehlers-Danlos and Marfan syndrome. Thus, careful refraction and correction are necessary to prevent amblyopia in childhood and improve visual acuity throughout life. Because of the progressive nature of these diseases, refraction may need to be repeated biannually. Additionally, the significant astigmatism seen with these corneal ectasias can be addressed with frequent corneal topography and the use of rigid contact lenses (Maumenee 1978; Wisenthal et al. 2013). Specifically for the management of the brittle cornea seen in Ehlers-Danlos syndrome type VI, early diagnosis is key in order to prevent corneoscleral rupture. However, if this were to occur, patch grafts may be used for repair (Wisenthal et al. 2013). For Marfan syndrome, lens subluxation may be treated with cataract extraction and may require the use of advanced surgical techniques, such as capsular tension rings, scleral fixation, or pars plana lensectomy (Wisenthal et al. 2013).

The goal of therapy for peripheral ulcerative keratitis seen in autoimmune connective tissue disorders is to decrease corneal melting, and this may be achieved with topical lubricants or bandage contact lenses to improve wetting and promote epithelialization, topical antibiotics as prophylaxis against infection, and topical or oral anti-collagenase drugs such as oral doxycycline to slow corneal thinning (Kanski and Bowling 2011). Topical corticosteroids, however, have variable effects and should be used with caution with significant corneal thinning (Wisenthal et al. 2013). Additionally, systemic high-dose

steroids can be used to control acute disease, while cytotoxic or immunomodulatory immunosuppressive agents, such as cyclophosphamide, azathioprine, mycophenolate mofetil, and methotrexate, may be required for longer-term disease management (Kanski and Bowling 2011). Biologic medications, such as infliximab, have also been shown to have some benefit in more severe cases (Wisenthal et al. 2013). In cases that are refractory to the above medical management, PUK may be surgically managed with conjunctival excision, corneal gluing or amniotic membrane patching for perforations, or keratoplasty for more diffuse corneal involvement (Kanski and Bowling 2011).

Prognosis

The corneal manifestation of both Ehlers-Danlos and Marfan syndrome are lifelong conditions that may continue to progress with time. If refraction is at an early age and at frequent intervals to keep up with this progression, patients with the corneal ectasias seen in these diseases may have visual acuities that are correctable with simple spectacle or contact lens wear. EDS type VI patients with the severe brittle cornea, however, are at risk for corneal perforation, and as such, care must be taken when performing intraocular surgery on them (Kanski and Bowling 2011; Wisenthal et al. 2013).

Unlike the above chronic conditions, peripheral ulcerative keratitis seen in autoimmune connective tissue disease has a more waxing and waning course, often only manifesting when there is decreased control of the systemic disease process. Thus, if systemic autoimmune disease is controlled, patients often have less PUK flares and good visual outcomes. When active, if PUK is treated appropriately, visual prognosis is related to the severity of the involved cornea with more extensive involvement leading to possible scar formation. If treated inadequately, however, a high proportion suffers from keratolysis or significant and rapid stromal melting with perforation, a severe disease-related morbidity (Wisenthal et al. 2013).

Epidemiology

Ehlers-Danlos syndrome affects approximately 0.02% of the population, and EDS type VI or the ocular-scliotic type is exceedingly rare, with fewer than 60 cases reported (Jacobson et al. 1997; Long et al. 2013). Marfan syndrome also affects approximately 0.02–0.03% of the population, though ophthalmic manifestations, notably subluxation of the lens, are very common in these patients, occurring in 80% of them. All autoimmune connective tissue diseases affect approximately 8% of the population, 78% of whom are women (Jacobson et al. 1997).

Cross-References

- ▶ Angioid Streaks – Ehlers-Danlos Syndromes
- ▶ Marfan Syndrome

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Contact Dermatitis

- ▶ Contact Dermatoblepharitis
- ▶ Dermatitis

Contact Dermatoblepharitis

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Synonyms

Allergic dermatitis; Contact dermatitis

Definition

Acute or chronic inflammatory reactions that occur after coming into contact with topical ophthalmic medications, cosmetics, systemic medications, or environmental substances.

Etiology

Systemic contact with a sensitizing agent or medicaments such as topical ophthalmic medications and cosmetics is very common (Peralejo et al. 2008). Any agent via a topical, cutaneous, oral, inhaled, intravenous, or environmental exposure can trigger a local allergic reaction. Industrial chemicals such as nickel, cobalt, and balsam of blue have also been implicated in systemic contact dermatitis. These agents cause an acute anaphylactic reaction or can be delayed 24–72 h. The acute reaction is from a type I IgE-mediated hypersensitivity reaction. The delayed reaction is due to a type IV T-cell-mediated hypersensitivity.

Clinical Presentation

The type I immediate hypersensitivity reactions typically occur within minutes after the first time being exposed to an allergen. This exposure results in itching, eyelid erythema and swelling, and conjunctival injection and chemosis. Instillation of topical anesthetics and antibiotics such as bacitracin, cephalosporins, penicillin, sulfacetamide, and tetracycline are common offenders. This often resolves spontaneously. Rarely, patients may have systemic anaphylaxis.

The delayed type IV hypersensitivity reactions usually occur 24–72 h following contact with the offending agent. These patients have often been sensitized to the offending agent from prior exposure. They experience an acute eczema with erythema, leathery thickening, and scaling of the eyelids. Other sequelae of chronic irritation include hyperpigmentation, dermal scarring, and lower eyelid ectropion. Papillary conjunctivitis and a mucoid or mucopurulent discharge may occur, in addition to punctate epithelial erosions (Suurmond 2009). Common medications include:

1. Cycloplegics (atropine, homatropine)
2. Aminoglycosides (neomycin, gentamicin, tobramycin)
3. Antivirals (idoxuridine, trifluridine)
4. Preservatives (thimerosal, ethylenediaminetetraacetic acid [EDTA], BAK)

Cosmetics deserve a special mention. Mascara and other products applied around the eyes have been reported for cases of allergic dermatitis. Mascara contains emulsifiers such as sodium borate and ammonium stearate, which can irritate the conjunctiva. Eye shadow makeup contains ditertiarybutyl hydroquinone, yellow D & C No. 11 dye, and diisopropanolamine. Nail polish can also cause contact dermatitis when the nails come into contact with the eyelids.

Diagnostics

Clinical exam
Patch testing to help identify the offending agent
Skin culture
Skin biopsy

Differential Diagnosis

Differential diagnosis includes vernal conjunctivitis, bacterial and viral conjunctivitis, cutaneous pemphigoid, and atopic disease.

Prophylaxis

Avoidance of offending agents.

Therapy

Identification and discontinuation of the offending agent are usually required. Most cases resolve with cool compresses and artificial tears. Adjunctive therapy includes topical antihistamines, mast-cell stabilizers, and nonsteroidal anti-inflammatory agents (NSAIDs). A short course of mild topical corticosteroids and topical tacrolimus can be applied to the eyelids and periocular skin as well. The use of topical vasoconstrictors can provide acute symptomatic relief, but should not be used long term (Sutphin et al. 2012–2013). An avoidance diet has also been shown to be effective in both adults and children (Matiz and Jacob 2011).

Prognosis

This is typically a self-limited condition and should resolve with discontinuation of the offending agents.

Epidemiology

Type I hypersensitivity reaction, occurs acutely.

Type IV hypersensitivity reaction, occurs 24–72 h after exposure.

Slight female predominance.

Cross-References

- ▶ Atopic Dermatitis
- ▶ Conjunctivitis
- ▶ Pemphigoid, Cicatricial
- ▶ Steroids

References

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Contact Lens-Induced Conjunctivitis

▶ Giant Papillary (Contact Lens-Induced) Conjunctivitis Disease

Continuous Curvilinear Capsulorhexis (CCC)

▶ Anterior Capsulorhexis

Contracted Socket

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Definition

Fibrosis of the anophthalmic socket with subsequent volume loss, mucosal lining deficit, and eyelid malposition resulting in varying degrees of disfigurement and the inability to maintain an ocular prosthesis.

Etiology

Socket contracture typically occurs following evisceration or enucleation, especially in the absence of an orbital implant, but can also occur in congenital anophthalmos. It may be more severe in cases of severe traumatic injury, previous reconstructive surgery, chemical burns (particularly alkali), radiotherapy, active cicatrizing conditions (Stevens-Johnson, ocular cicatricial pemphigoid), or chronic inflammation from an ill-fitting implant/prosthesis.

Clinical Presentation

Several classification schemes have been developed but none have gained wide acceptance. Recently a review by Tawfik et al. (2009) proposed the following:

Grade 1

Minimal or no contraction of the inferior and/or superior fornices with an inability to maintain an ocular prosthesis over time. Usually presents with horizontal lid laxity, associated entropion/ectropion, and shortened or prolapsed inferior fornix. Also includes patients with an oversized or displaced orbital implant.

Grade 2

Mild contracture of the inferior and/or superior fornices with an inability to maintain a prosthesis over time. May have associated eyelid malposition as in *group 1*.

Grade 3

More advanced scarring than *grade* 2 with near-complete contracture of the inferior and/or superior fornices. Inability to place a prosthesis.

Grade 4

Severe vertical and horizontal contracture of the palpebral fissure. Also includes cases of recurrence after reconstructive surgery and irradiated sockets.

Differential Diagnosis

Microphthalmos
Anophthalmos

Therapy

The basic goals of reconstruction are excision of fibrotic tissue and replacement of the lost conjunctiva with grafts or flaps. Vascularization of the orbit may be compromised due to scarring. Contraindications to socket rehabilitation include multiple failed attempts at reconstruction, extensive fibrosis, massive injury, and chronic infection. The presence of severe eyelid malposition may be a relative contraindication as an aesthetically acceptable result may not be attainable even after successful socket reconstruction.

Grade 1

A lower lid tightening procedure, i.e., lateral tarsal strip, may be sufficient to correct lower lid laxity. If inferior fornix prolapse persists, fornix-forming sutures may be required. In more advanced cases, posterior lamellar augmentation via spacer grafts may be beneficial. If shallowing of the fornix is due to an oversized or migrated implant, explanting and resizing of the implant are usually adequate.

Grade 2–3

Amniotic membrane or mucous membrane grafts may be used in mild to moderate cases of socket contracture. Amniotic membrane acts as a "substrate" in that it requires healthy adjacent conjunctival epithelium to migrate, differentiate, and multiply over the graft to repair the mucosal lining deficit. Advantages include wide availability, anti-fibroblastic properties, and the avoidance of donor site morbidity. Furthermore, recent studies show comparable efficacy to mucous membrane grafts. Mucous membrane is still a viable option and acts as a "substitute graft," obviating the need for healthy adjoining conjunctiva. Should a concomitant volume deficit be present, implantation of a

dermis fat graft may be more appropriate. Please refer to the chapter on *Dermis Fat Graft* for more information on this topic. After prosthesis fitting, associated eyelid malposition may then be corrected as described above.

Grade 4

The repair of the severely contracted socket is complex and often requires a multidisciplinary approach. Current options include radial forearm free flaps, thoracodorsal artery trilobed adiposal flaps, retroauricular fasciocutaneous flaps, and temporalis fascia flaps. Acquired orbital bony deformities should be concurrently repaired. C- or U-shaped osteotomies and bone grafts may be used to expand the orbit. Interestingly, one recent case report used a high-density polymethylene methylacrylate orbital expander, typically an approach used in the treatment of congenital anophthalmos, in an irradiated socket that had been deemed inoperable. After six seeks, the socket was completely epithelialized, and the fornices were sufficiently deep to accommodate a prosthesis.

Cross-References

- ▶ Amniotic Membrane Graft
- ▶ Buccal Mucous Membrane Graft
- ▶ Dermis-Fat Grafts
- ▶ Eyelid Trauma
- ▶ Implants, Orbital
- ▶ Nanophthalmos

Further Reading

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Contrast Sensitivity

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Synonyms

Photometric contrast sensitivity

Definition

The contrast sensitivity represents the visual system's ability to detect differences in photometric brightness in the visual field (Bach et al. 2008).

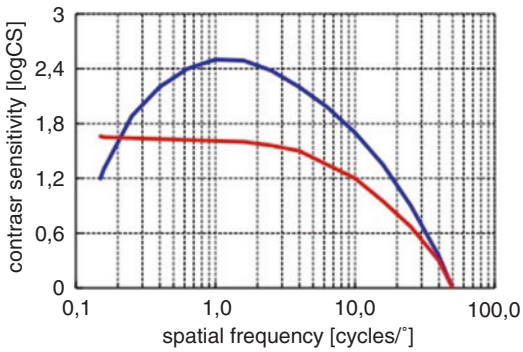
Basic Characteristics

Contrast is defined as a defined ratio of photometric brightnesses.

For the evaluation of CS, optotypes of the same size but with decreasing contrast are used. This contrast, used to characterize small objects in monochromatic surrounding area, is called Weber contrast. Formula 1 defines the respective ratio:

$$CSW = \frac{L_i - L_u}{L_u}$$

L_i is the optotypes photometric brightness [cd/m^2], whereas L_u is the photometric brightness of the surrounding area. Another option is to characterize contrast which changes progressively within the visual field. Respective optotypes can be Gabor patches, which display sinusoidal brightness distributions. This contrast is called Michelson contrast:



Contrast Sensitivity, Fig. 1 Contrast sensitivity function (CSF)

$$CSW = \frac{L_{max} - L_{min}}{L_{max} + L_{min}}$$

L_{max} is the maximum brightness and L_{min} is the minimum brightness. This concept has been derived from the fact that the visual system uses different channels for the detection of optotypes of different sizes. L of course depends on luminous intensity [cd] and thus on surrounding light conditions, which is why contrast sensitivity testing has to be performed separately for photopic and different mesopic conditions.

Contrast sensitivity is the reciprocal value of the smallest detectable photometric contrast (contrast threshold). If a contrast of 1 percent is noticeable, the CS is 100 or 2 log CS (10^2). Plotting CS as a function of object size/spatial frequency for sinusoidal patterns results in the contrast sensitivity function (CSF). The CSF shows that CS depends on object size and is rapidly decreasing for decreasing object size (Fig. 1). In reverse, for detection of small optotypes, a maximum contrast is needed. The smallest value of the CSF on the right end of the function represents visual acuity.

Cross-References

► ETDRS Visual Acuity Chart

References

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Contrast Sensitivity Function, General

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Synonyms

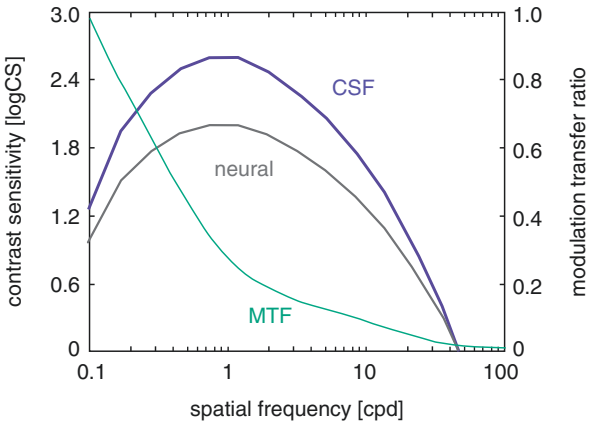
CSF

Definition

The function that characterizes contrast sensitivity as a function of spatial frequency (object size).

Basic Characteristics

The visual system's ability of recognizing objects of different contrasts is dependent from the size of the object. This ability – known as contrast sensitivity – is characterized by the contrast sensitivity function (CSF) (Richman et al. 2013). The CSF is a result of the modulation transfer function (MTF) that depicts the loss of contrast as a function of spatial frequency through a given optical system and the neural contrast sensitivity function (nCSF) that describes the contrast sensitivity of the neural component of the visual system (Fig. 1). The result of both functions is a bell-shaped curve for sinusoidal gratings and a flat-shaped curve for optotypes (Fig. 2). The CSF can be determined psychophysically either by measuring contrast thresholds at different spatial frequencies (optotype sizes) or by measuring visual acuity

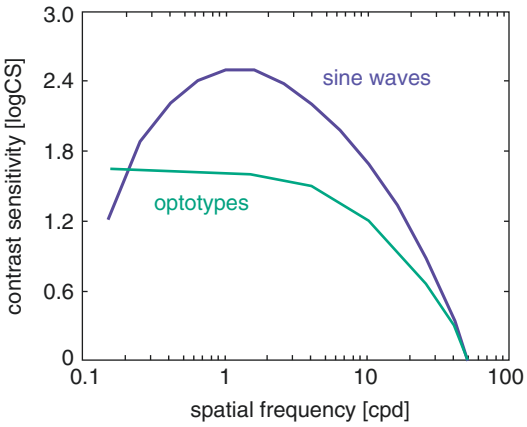


Contrast Sensitivity Function, General, Fig. 1 Schematic drawing showing the relations between the contrast sensitivity function (*CSF*), the neural contrast sensitivity function (*nCSF*), and the modulation transfer function (*MTF*)

with optotypes of different contrast. While the CSF has typical values in normal subjects, there is a high interindividual variability.

Pathological conditions can affect the CSF and reduce contrast sensitivity. Aberrations, scatter, and diffraction decrease the MTF. Typical diseases in this group are cataract, corneal scars, keratoconus, and status post-refractive surgery. Other diseases such as optic neuropathies or neural diseases affect the nCSF.

Traditionally, the CSF is measured using sinusoidal gratings of different spatial frequencies. Nowadays, in clinical practice and for scientific purposes, often only parts of the CSF such as the (presumed) peak value are measured (Pelli et al. 1988; Rabin and Wicks 1996), although grating-based tests are still popular. The cutoff spatial frequency at maximum contrast equals visual acuity.



Contrast Sensitivity Function, General, Fig. 2 Schematic drawing showing the contrast sensitivity function (*CSF*) for sine wave gratings and for optotypes (e.g., letters)

Cross-References

► Pelli-Robson Chart

References

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Contusion

► Eyelid Trauma

Core Vitrectomy

► Vitrectomy

Cornea

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Definition

The cornea is the transparent front part of the eye that covers the iris, pupil, and anterior chamber consisting of highly specialized tissue. The difference of refractive indices between air and tear film/cornea renders the cornea the part with the highest dioptric power in the optical system of the eye (ca. 43 D). The average cornea is ca. 0.5 mm thick and consists of five layers (corneal epithelium, Bowman's layer, corneal stroma, Descemet's layer, corneal endothelium). The corneal epithelium is of ectodermal origin; the other layers are of mesodermal origin.

Cross-References

- ▶ Corneal Dystrophies of Bowman's Layer (CDB), Reis-Bücklers Dystrophy, Thiel-Behnke Dystrophy
- ▶ Corneal Endothelium Image
- ▶ Corneal Stromal Haze
- ▶ Descemet's Membrane Endothelial Keratoplasty (DMEK)
- ▶ Stem Cells, Limbal, Corneal Epithelium Maintenance
- ▶ Wavelength-Dependent Refractive Index

Cornea Farinata

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Synonyms

Floury Cornea

Definition

This condition is characterized by fine, multiple, usually bilateral, punctate, and tan-to-white- or gray-white-colored dots localized in the deep central posterior stroma just anterior to Descemet's layer. The deposits can be visualized at the slit lamp and are visually asymptomatic. Ocular treatment is not necessary. The opacities are best visualized with retroillumination of the iris (Rapuano and Heng 2012).

Etiology

The cause is unknown, but the histophatology suggests that they are composed of a lipofuscin-like substance in stromal keratocytes (Yanoff and Duker 2014; Tratller et al. 2010). It was first described by Vogt in 1923 (Yanoff and Duker 2014; Durand et al. 1990). Cornea farinata may result from mutations (at least six) in the steroid sulfatase gene (STS), but they have not been correlated with the presence or absence of corneal abnormalities (Klintworth 2003).

Occurrence

Cornea farinata is a relatively common degenerative condition presenting in the cornea of elderly patients (Yanoff and Duker 2014; Rapuano and Heng 2012).

Classification

Corneal confocal microscopy can be used to help with classification of the disease differing it from deep filiform dystrophy, posterior punctiform dystrophy, punctuate dystrophy, pre-Descemet's dystrophy, and fleck dystrophy. These corneal dystrophies are all characterized by the presence of fine opacities at the posterior corneal stroma. In patients with cornea farinata, the superficial and mid-stroma layers are normal on confocal microscopy, and in the deep stroma can be found highly reflective small particles in the cytoplasm of

keratocytes. The endothelial cells and the Descemet's membrane are normal (Kobayashi et al. 2003).

Cross-References

► Corneal Degenerations

References

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Cornea Plana

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Definition

Cornea plana is a bilateral inherited disorder of the cornea which typically presents with a small flat cornea, hyperopia, and a shallow anterior chamber (Nischal and Sowden 2003; Gupta and Kim 2011).

Etiology

Cornea plana is an inherited disease which can be autosomal dominant (AD) or autosomal recessive (AR) (Gupta and Kim 2011). The genes localize to the long arm of chromosome 12 with mutations in the KERA genes being implicated (Gupta and Kim 2011). Many consider cornea plana and sclerocornea to be part of the same spectrum (Nischal and Sowden 2003).

It has been postulated that there is an absence of the limbal anlage (Nischal and Sowden 2003). The limbal anlage is the structure responsible for both limbal differentiation and corneal curvature. The formation of the limbal anlage occurs during the seventh to tenth gestational weeks and aids the differentiation of neural crest cells into either sclera or cornea (Nischal and Sowden 2003). This differentiation is critical because it allows the corneal curvature to exceed the scleral curvature. In the absence of the normal differentiation of the sclera and cornea, the corneal curvature is flattened.

Clinical Presentation

Two types of cornea plana exist: CNA1 is the less severe form which is usually inherited in an AD fashion and CNA2 is the more severe form which is usually AR (Nischal and Sowden 2003; Sugar and Wadia 2009; Gupta and Kim 2011). Patients classically present with flat corneas which have keratometry readings of less than 43 diopters, but some may have corneas as flat as 20 diopters. The recessive and dominant forms share clinical signs such as reduced corneal curvature, indistinct limbus, and arcus lipoides at an early age. In the autosomal dominant cornea plana, the corneal refractive power is reduced to 38–42 D, whereas in autosomal recessive cornea plana, corneal refractive power is reduced to 23–35 D. The anterior chamber is usually shallow, which can predispose patients to acute angle-closure glaucoma.

On clinical exam, patients can be both highly hyperopic or myopic, depending on the presence of other ocular abnormalities. Obscuration of limbal landmarks and peripheral scleralization of the cornea is usually present, which can make it difficult to distinguish from peripheral sclerocornea.

Cornea plana can be associated with other concurrent anterior segment abnormalities, including iris colobomas, congenital cataract, and occasional posterior segment colobomas (Nischal and Sowden 2003).

Diagnosis

Clinical evidence of corneal flattening without significant corneal opacification.

Differential Diagnosis

1. Sclerocornea
2. Microcornea
3. Posterior embryotoxin
4. Glaucoma
5. Peter's anomaly

Therapy

Management consists of cycloplegic refraction and correction of refractive error, as well as close follow-up for glaucoma surveillance (Nischal and Sowden 2003; Gupta and Kim 2011).

Prognosis

The prognosis is variable. Vision may be limited by amblyopia, glaucoma progression, or other congenial ocular malformations.

Epidemiology

Rare, it was first described by Rubel in 1912 as congenital familial flatness of the cornea. Many of the first families were from Finland, but since then families of Chinese, Saudi Arabian, and British origin have been described.

Cross-References

► Sclerocornea

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Cornea Verticillata

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Synonyms

Cornea verticillata of Fleischer; Hurricane keratopathy; Vortex keratopathy

Definition

Corneal epithelial pigmented deposits in a linear whorl-like pattern.

Etiology

Cornea verticillata can be drug induced or a manifestation of Fabry disease. In drug-induced cornea verticillata, the underlying pathology is attributable to the diffusion of amphiphilic medication into cell lysosomes. Once within lysosomes, the drug binds phospholipids preventing their enzymatic degradation and leading to an accumulation of lysosomal inclusions within corneal epithelial cells. Similarly, in Fabry disease, an X-linked disorder of reduced alpha-

galactosidase A activity, trihexosylceramide accumulates and forms lysosomal inclusions within corneal epithelial cells (Hollander and Aldave 2004). Shearing forces from the upper lid result in preferential loss of corneal epithelial cells at the apex, thus stimulating the centripetal migration of lysosomal deposit-laden limbal epithelial cells to the central cornea. This forms a whorl of lines extending from the limbus to the center in a curving, clockwise pattern. The lines have a clockwise predisposition due to the ocular electromagnetic field's influence on migrating epithelial cells (Dua et al. 1996). These lines concentrate in the inferior cornea just below the limit of excursion of the upper lid.

Clinical Presentation

Cornea verticillata is typically an incidental finding and is asymptomatic. Rarely, patients may notice haloes. Findings are usually bilateral and located inferiorly. The epithelial deposits appear as grayish or golden-brown opacities that branch out from a central whorl. In patients with drug-induced corneal verticillata, a history of taking an amphiphilic drug such as amiodarone, chloroquine, indomethacin, and phenothiazines is usually present (D'Amico et al. 1981). In patients with Fabry disease, other systemic manifestations such as pain (acroparesthesia), kidney failure, cardiomyopathy, and skin angiokeratomas are usually present. Females can show a wide range of clinical manifestations, although symptoms are typically less severe and of later onset than hemizygous males (Deegan et al. 2006).

Diagnosis

Patients have a history of amphiphilic medication use or signs of symptoms of Fabry disease, which can be diagnosed by an enzyme assay to measure level of alpha-galactosidase activity. Slit-lamp examination shows characteristic corneal epithelial deposits in a vortex-like pattern. Recently, confocal laser scanning microscopy has been used to characterize and differentiate the deposits in Fabry and drug-induced corneal verticillata (Falke et al. 2009). It was also helpful in detecting corneal changes in Fabry disease prior to their appearance on slit-lamp biomicroscopy and in monitoring the response to treatment.

Differential Diagnosis

- Striate melanokeratosis (seen in black individuals with heavy limbal pigmentation after corneal epithelial injury)
- Epithelial iron lines
- Stromal deposits (gold, silver, retinoid depositions)
- Adrenochrome deposits in the cornea

Prophylaxis

None.

Therapy

There is no recommended treatment for drug-induced corneal verticillata, and the offending medication is typically not stopped based on the presence of these deposits. However, in rare cases, if patients are symptomatic, the medication can be stopped. Keratopathy can take months to resolve after cession of medication. Fabry disease is treated with enzyme replacement therapy.

Prognosis

Excellent with no visual involvement in most cases. When the inciting drug is stopped, most cases of corneal verticillata eventually fade away.

Epidemiology

Corneal verticillata is present in 69–100% of patients taking amiodarone (Hollander and Aldave 2004). The duration and dosage of drug ingestion correlate with the degree of cornea

involvement (D'Amico et al. 1981). The prevalence of cornea verticillata in Fabry disease varies between 44% and 94.5% in men and 88% in women (Falke et al. 2009). It is found in 70–80% of heterozygous female carriers.

Cross-References

- ▶ Chloroquine Toxicity, Cornea Verticillata
- ▶ Chlorpromazine, Cornea Verticillata
- ▶ Hurricane (Vortex) Keratopathy
- ▶ Vortex (Hurricane) Keratopathy

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Cornea Verticillata of Fleischer

- ▶ Cornea Verticillata

Corneal Aberrometry

- ▶ Wave Front Analysis

Corneal Ablation

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Synonyms

Keratectomy; Keratomileusis

Definition

Corneal ablation is the removal of tissue over a defined region using a laser, typically an excimer laser.

History

In the 1980s Steven Trokel investigated the use of the excimer laser to remove fine layers of corneal tissue for the correction of ametropia. Excimer lasers emit light in the UV range. In contrast to many lasers in the visible range such as the argon laser, the excimer laser does not induce thermal effects on the tissue but disrupts the molecular bonds leading to a disintegration ("vaporization") of surface tissue with minimal collateral damage. This characteristic allowed a novel type of extremely precise (µm range) and highly reproducible tissue engineering, the excimer laser ablation. The classical domain of the excimer laser is corneal refractive surgery; however it has been used in keratoplasty in the pre-femtosecond laser era (Seitz et al. 1999). Excimer ablations have also been performed for trabecular meshwork surgery (Wilmsmeyer et al. 2006). Besides living tissue also materials (e.g., poly(methyl-methacrylate) (PMMA)) can be treated with excimer lasers. The use of solid-state lasers instead of (gas-based) excimer lasers is still experimental.

Clinical Features

The surgical-technical performance of a laser ablation requires a specially adapted laser

(excimer laser). The laser beam is delivered using a system of mirrors and apertures for correctly shaping the ablation. An eye tracker system guarantees the ablation taking place exactly at the planned location. The procedure itself is short. The ablation time varies from a few seconds to more than a minute and depends from the number of pulses and from the repetition rate of the laser. Modern excimer lasers have a frequency of up to 750 Hz. The ablation causes only negligible thermal effects but fumes that need to be removed from the operation area. After first-generation photorefractive keratectomy (PRK) procedures, the ablated area could be identified by diffuse whitish scar tissue (haze). In modern corneal excimer refractive surgery, the ablation zone can only be identified using corneal topography.

Tests

The effects of corneal ablation can be checked with pachymetry and, more precisely, with corneal topography and aberrometry. Particularly corneal topography allows visualization over magnitude and centration of the ablation zone on the cornea. There are different concepts of a closed-loop excimer corneal ablation. Real-time interferometry allows monitoring the change of corneal shape during the ablation procedure (Schruender et al. 2002). Optical coherence pachymetry (OCP) continuously measures central corneal thickness (Wirbelauer and Pham 2004). While the interferometric approach did not emerge from an experimental stage, some laser platforms are offered with an OCP unit. For the investigation of wound healing effects after excimer laser ablation, confocal in vivo microscopy is the method of choice.

Cross-References

- ▶ Decentration
- ▶ Excimer Lasers
- ▶ Photorefractive Keratectomy (PRK)

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Corneal Abrasion

- ▶ Epithelial Defects
- ▶ Epithelial Erosions

Corneal Arcus

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Synonyms

Anterior embryotoxon; Arcus juvenilis; Arcus senilis; Gerontoxon

Definition

Corneal arcus represents a degenerative process of lipid deposition in the peripheral cornea. It is characterized by a circumferential gray-white or yellow band within the corneal stroma, Bowman's

membrane, and Descemet's membrane, with the sparing of corneal epithelium.

Arcus often begins in the inferior, then superior perilimbal cornea, and eventually coalesces to form a complete ring 1 mm in width. A 300 μm wide clear zone separates its peripheral border and the limbus, a space known as the "lucid interval of Vogt." This interval may be due to lipid reabsorption by limbal vasculature; rarely, it may undergo mild thinning and develop into senile furrow. The arcus has a sharp peripheral border ending at the edge of Bowman's membrane and a diffuse central border which may show crossing dark lines of reduced lipid deposition. The arcus is densest and widest superiorly. It is almost always bilateral but may be asymmetric with decreased arcus secondary to ipsilateral carotid vascular disease or increased arcus in association with chronic hypotony.

Histology reveals lipid concentration within anterior and posterior stroma organized in an "hourglass" pattern. This arrangement extends into the corneal stroma from Bowman's and Descemet's membranes. Deposits initially occur in the deep stroma and later superficially, with least density in the mid stroma (Agarwal et al. 2002; Cavallotti and Cerulli 2008; Kanski and Bowling 2011; Krachmer et al. 2011; Yanoff and Duker 2013).

Etiology

In corneal arcus, deposits are made up of cholesterol, cholesterol esters, phospholipids, and neutral glycerides. The predominant lipid consists of extracellular cholesteryl ester-rich particles. Initial deposition forms as a double lamina in the anterior layers of Descemet's membrane. It then deposits and remains within Bowman's membrane without further progression. In advanced stages, deposition may occur between the stromal lamellae, with sparing of the limbus.

Formation of the corneal arcus is related to increasing age, proximity of blood vessels to the peripheral cornea, increased vessel permeability, and hypercholesterolemia, particularly in association with low-density lipoprotein (LDL). The permeability of limbal vessels increases with age. This allows LDL to pass into the corneal stroma from limbal capillaries. In the presence of elevated circulating LDL, the tight junctions formed by the endothelium of limbal vasculature may become dysfunctional. This may also contribute to the passage of vascular LDL into the cornea. The accumulating LDL may transform into a modified LDL and apolipoprotein B. Corneal arcus and atherosclerosis are both related to the level of LDL in the plasma.

Corneal deposits may also occur as a result of rare genetic disorders of high-density lipoprotein (HDL) metabolism. These include lecithin cholesterol acyltransferase (LCAT) deficiency (Norum disease), fish-eye disease, and Tangier disease. These diseases may manifest at an early age and cause corneal clouding which may affect visual acuity. Corneal arcus is also associated with osteogenesis imperfecta type I, Schnyder crystalline corneal dystrophy, myxedema, and Bassen–Kornzweig syndrome (abetalipoproteinemia) (Kanski and Bowling 2011; Krachmer et al. 2011; Yanoff and Duker 2013).

Occurrence

Corneal arcus is the most common of the corneal degenerations. In men, it occurs with increasing frequency between 40 and 80 years of age, affecting 90% of men between 70 and 80 years of age, and nearly 100% of men older than 80 years of age. A similar pattern is seen in women, with a delay of approximately 10 years. Occurrence is also associated with ethnicity; persons of African descent develop arcus most frequently and at a younger age than individuals of other racial origins.

Although arcus senilis generally has no visual significance, premature formation (arcus juvenilis) can be associated with hypercholesterolemia,

particularly in men under 50 years of age. Young patients with arcus have an increased risk for type IIa and less commonly for type IIb hyperlipoproteinemia, but a decreased risk for type IV hyperlipoproteinemia. In addition to corneal arcus, these patients may have systemic signs such as xanthelasma. Men with arcus juvenilis also have a fourfold increased relative risk of mortality from coronary heart disease and cardiovascular disease. Patients with corneal arcus under 50 years of age should undergo lipid profile and cardiovascular evaluation. Corneal arcus in older patients does not correlate with mortality, including those with diabetes.

Arcus juvenilis may also occur in children with familial hyperlipoproteinemia, megalocornea, keratoconus, atopic or vernal keratoconjunctivitis, osteogenesis imperfecta, or blue sclera (Cavallotti and Cerulli 2008).

Classification

Corneal arcus is given different designations based on the age of presentation. Arcus senilis or gerontoxon refers to corneal arcus in the aging population of older than 50 years of age. Arcus juvenilis or anterior embryotoxan occurs in individuals younger than 50 years of age and is primarily due to hyperlipidemia.

Similar lipid deposition may occur in the perilimbal sclera overlying the ciliary body; this may be considered to be a lipid keratopathy rather than corneal arcus (Krachmer et al. 2011).

Cross-References

- ▶ Blue Sclera
- ▶ Crystalline Dystrophy
- ▶ Furrow Degeneration, Senile
- ▶ Lipid Keratopathy
- ▶ Megalocornea
- ▶ Osteogenesis Imperfecta, Blue Sclera
- ▶ Xanthelasma, Dyslipoproteinemia
- ▶ Xanthomas

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Corneal Astigmatism

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Synonyms

General: astigmatism

Definition

The term corneal astigmatism describes different corneal curvatures along two orthogonal meridians. It is a result from anterior and posterior surface astigmatism. In most cases, a small amount of corneal astigmatism (ca. 1 D) is present with the steep axis at 90° (astigmatism with the rule). This corneal astigmatism is compensated for by lenticular (internal) astigmatism with the steep axis at 0°. Corneal astigmatism can be visually significant if its magnitude exceeds the magnitude of compensating internal astigmatism. Corneal astigmatism can be very high in cases of keratoconus and after penetrating keratoplasty.

Cross-References

- ▶ Astigmatism
- ▶ Keratoconus

Corneal Collagen

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Synonyms

Corneal protein fibrils

Definition

Fibrous protein of the cornea.

Structure

Collagen molecules in the corneal stroma form triple-helix collagen fibers; arranged in bundles, these collagen fibers form collagen lamellae. There are at least 12 types of collagen present in the cornea, the most commonly found being type I (Gipson et al. 2005).

Function

Corneal transparency and biomechanical properties depend on and are maintained by the ordered alignment of its collagen fibrils, which are arranged in parallel, thus forming the scaffolding of the cornea (Maurice 1957). In the posterior two thirds of the human cornea, collagen lamellae are found in the plane of the cornea stretching from limbus to limbus with some degree of anteroposterior interweave. At the limbus, the collagen fibrils follow a circular course, while in the anterior stroma, a considerable anteroposterior interweave is found (Morishige et al. 2011).

Collagen makes up 71% of the dry weight of the cornea (Gipson et al. 2005).

Clinical Relevance

In the cornea, collagen is present in the epithelial and endothelial basement membranes, the Bowman's layer, and the stroma. The organization of corneal collagen is key to the maintenance of corneal curvature. Keratoconus, in which the corneal shape is compromised, is known to be associated with the displacement of the axes of the collagen fibrils (Meek et al. 2005).

Cross-References

- ▶ Cornea
- ▶ Corneal Degenerations
- ▶ Corneal Ectasia
- ▶ Keratoconus
- ▶ Pellucid Marginal Corneal Degeneration

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Corneal Defect

- ▶ Epithelial Defects

Corneal Degenerations

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Definition

Corneal degenerations are a group of sporadic and age-related corneal conditions that are present in previously normal corneal tissue and occur most often near the limbus.

Basic Characteristics

Degenerative corneal processes are characterized by secondary changes in previously normal corneal tissue. Compared to corneal dystrophies, degenerative processes are not inherited, usually affect more than one corneal layer, and are asymmetric, unilateral, and usually peripheral. Often corneal degeneration is associated to neovascularization and inflammation.

There are many corneal degenerative conditions including Salzmann's nodular degeneration, calcific band keratopathy, lipid keratopathy, actinic keratopathy, pannus, and bullous keratopathy.

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Corneal Diameter

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Synonyms

White-to-white distance

Definition

Horizontal measurement across the cornea.

Structure

At birth, a normal human cornea measures 10 mm in horizontal diameter, whereas the size of a normal adult cornea measures approximately 12 mm horizontally, practically always exceeding the vertical diameter. Adult corneal diameter is reached at 2 years of age (Velazquez 2005; Friedman 2007).

Function

To rule out disorders associated with anomalies of the size and shape of the cornea such as buphthalmos in children and to assess biometrical parameters of the anterior chamber prior to intraocular surgery.

Measurements can be performed with a variety of devices such as partial coherence laser interferometry or optical coherence tomography.

Clinical Relevance

Corneal diameter measurements are of importance in disorders such as microcornea,

megalocornea, buphthalmos, and other corneal dystrophies.

Preoperative WTW distance is required in choosing an intraocular lens (IOL), as the calculation of an optimally sized angle-fixated anterior chamber IOL or sulcus-supported posterior chamber IOL depends on horizontal WTW (Velazquez 2005).

Cross-References

- ▶ Megalocornea
- ▶ Microcornea
- ▶ Microphthalmos (Microphthalmia)
- ▶ Phakic Intraocular Lens
- ▶ PRL Phakic Intraocular Lens
- ▶ Verisyse Iris-Supported Phakic Intraocular Lens

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Corneal Dystrophies

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Synonyms

Anterior or superficial dystrophies

Anterior corneal dystrophy, Epithelial basement membrane dystrophy (EBMD), Map-dot-fingerprint dystrophy, Cogan microcystic dystrophy
Meesmann dystrophy
Lisch corneal dystrophy
Corneal dystrophies of Bowman's layer (CDB), Reis-Bücklers dystrophy, Thiel-Behnke dystrophy

Stromal dystrophies

Granular dystrophy, Avellino dystrophy, Groenouw dystrophy type I
Lattice dystrophy type I, Biber-Haab-Dimmer
Lattice dystrophy type II, Meretoja syndrome
Macular corneal dystrophy (MCD)
Polymorphic stromal dystrophy
Schnyder crystalline corneal dystrophy
Crystalline corneoretinal dystrophy (Bietti)
Congenital hereditary stromal dystrophy
Fleck dystrophy
Central cloudy dystrophy of François
Posterior crocodile shagreen

Posterior dystrophies

Congenital hereditary endothelial dystrophy (CHED)
Iridocorneal endothelial syndrome (ICE)
Fuchs endothelial corneal dystrophy (FECD)
Posterior polymorphous dystrophy (PPMD)

Definition

Inherited corneal diseases with a spectrum of findings and symptoms secondary to the location of the pathology.

Basic Characteristics

With rare exception, corneal dystrophies are bilateral, relatively symmetric, genetic conditions in which the pathology appears to be localized to ocular tissue. Dystrophies may be classified according to genetic pattern, severity of disease, histopathology, biochemical characteristics, or anatomical location. One of the most commonly employed classification systems is stratification according to the involved levels of the cornea:

anterior or superficial, stromal, and endothelial. A new classification system, IC3D classification of corneal dystrophies, was published in 2009 and combines traditional nomenclature with evolving genetic and clinicopathologic data. Specific symptoms, findings, and management of corneal dystrophies are dictated by the location and the progression of the pathologic findings.

Cross-References

- ▶ Bietti Crystalline Retinopathy
- ▶ Congenital Hereditary Endothelial Dystrophy
- ▶ Endothelial Dystrophies
- ▶ Epithelial Dystrophies
- ▶ Epithelial Erosions
- ▶ Fuchs Dystrophy
- ▶ Groenouw Dystrophy Type I
- ▶ Iridocorneal Endothelial Syndrome (ICE)
- ▶ Lattice Dystrophy
- ▶ Macular Dystrophy
- ▶ Map-Dot-Fingerprint Dystrophy
- ▶ Meesmann Dystrophy
- ▶ Meretoja Syndrome
- ▶ Posterior Corneal Dystrophies
- ▶ Recurrent Corneal Erosion
- ▶ Reis-Bücklers Dystrophy
- ▶ Schnyder Crystalline Dystrophy Syndrome
- ▶ Stromal Dystrophies
- ▶ Thiel-Behnke Dystrophy

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Corneal Dystrophies of Bowman's Layer (CDB), Reis-Bücklers Dystrophy, Thiel-Behnke Dystrophy

- ▶ Corneal Dystrophies

Corneal Dystrophy

- ▶ Endothelial Dystrophies

Corneal Dystrophy of Bowman's Layer, Type I (CDB I)

- ▶ Reis-Bücklers Dystrophy

Corneal Dystrophy of Bowman's Layer, Type II (CDB2)

- ▶ Thiel-Behnke Dystrophy

Corneal Ectasia

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Synonyms

Keratectasia; keratoectasia

Definition

A progressive thinning of the corneal stroma with subsequent increase of corneal curvature and induction of higher-order aberrations (HOA) due to irregular astigmatism. The origin of corneal ectasia can be a degenerative disease (keratoconus, pellucid marginal degeneration (Rabinowitz 1998)), a congenital anomaly (keratoglobus), or a mechanical trauma such as surgery (iatrogenic keratectasia (Seiler et al. 1998)). Ectasia due to other reasons (infection) is rare.

Histology

In all ectatic diseases, a stromal thinning can be observed. A recent histological study showed that

ruptures in Bowman's layer that are typical for keratoconus (KC) were absent in eyes with iatrogenic keratectasia (IK) (Meghpara et al. 2008). Immunohistochemical examinations revealed different expression patterns of α_1-proteinase inhibitor and matrix metalloproteinases (MMP) in KC and IK eyes. KC showed lower levels of α_1-proteinase inhibitor and higher levels of MMP-1 compared to normal eyes. Expression patterns in IK eyes were similar to those in normal eyes. These discrepancies suggest that KC and IK are two different entities.

Newer studies applying second harmonic imaging showed that in KC corneas the collagen lamellae in the anterior stroma were less interweaved, and there were less lamellae inserting into Bowman's membrane (Morishige et al. 2007).

Molecular Diagnostics

There are no valid molecular diagnostics available at the moment.

Electron Microscopy

In KC eyes, epithelial cells showed signs of degeneration and accumulation of ferritin (Fleischer's Ring). In the stroma, a reduction of collagen lamellae and deposits beneath the keratocytes can be detected. Also in Descemet's layer, ruptures were found (Vogt's Striae). In IK eyes, collagen fibril thinning and decreased interfibril distance were observed in the stromal bed.

Differential Diagnosis

The most important criterion for an ectatic disease is – by definition – a progressive thinning. In the early stage, all ectatic diseases are difficult to detect without corneal topography and optical pachymetry. Secondly, the differential diagnosis between different corneal ectatic diseases has to be made (e.g., KC vs. pellucid marginal degeneration).

Cross-References

- ▶ Keratectasia
- ▶ Keratoconus
- ▶ Keratoglobus
- ▶ Pellucid Marginal Degeneration

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Corneal Edema

▶ Hydrops, Keratoconus

Corneal Endothelial Rejection Line

▶ Khodadoust Line

Corneal Endothelium Image

▶ Photomicroscopy, Specular

Corneal Epithelial Cysts

▶ Microcystic Epitheliopathy

Corneal Erosion

▶ Epithelial Defects
▶ Epithelial Erosions

Corneal Graft Rejection

▶ Endothelial Graft Rejection

Corneal Guttata

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Definition

Corneal guttae are extracellular matrix excrescences in Descemet's membrane. The name gutta comes from Latin meaning "drop," and guttata is the adjective used to describe "drop-like." They resemble dewdrops on slit lamp examination and appear either as mushroom or as flat anvil profiles on histology preparations.

Etiology

It is believed that corneal guttae are the result of stressed or abnormal endothelial cells. These cells produce focal collagen accumulations that appear on the posterior surface of Descemet's membrane. The Descemet's membrane of the cornea is made of type IV collagen and has anterior banded and posterior nonbanded portions. This nonbanded portion may not be present in diseases like Fuchs dystrophy as the abnormal endothelial cells produce 110° banded portions (Vanmeter et al. 2013). This production of banded collagen is focal and is thought to be the cause of corneal guttae and Hassel-Henle warts (Vanmeter et al. 2013). Initially, guttae begin very small and are first seen on specular microscopy. Eventually, they grow and fuse together thus forming larger guttae and give the cornea a characteristic "beaten metal" appearance on slit lamp exam. These guttae disrupt the normal, orderly hexagonal mosaic of endothelial cells, which leads to increased size and irregularly shaped endothelium with a greater proportion of tetragonal and octagonal cells (Giasson et al. 2007; Weisenthal and Streeten 2011). This formation in the Descemet's membrane leads to endothelial cell dysfunction. This dysfunction can increase to cause edema and eventually clouding of vision (Giasson et al. 2007).

Occurrence

The finding of cornea guttae can be relatively common. They can be characteristic of a normal aging cornea and are found in the 6th, 7th, and 8th decades of life at rates of 6%, 12%, and 29%, respectively (Hillenaar et al. 2012). While the genetic basis and environmental factors have not been fully understood, there is geographic variation in guttae prevalence and differences among sexes (Giasson et al. 2007). Females have a frequency of guttae 2.5 times that of males in the setting of Fuchs dystrophy (Weisenthal and Streeten 2011). Smokers with a >20 pack-year smoking history also have over double the risk of corneal guttata (Zoega et al. 2006). Interestingly, higher body weight is associated with a lower risk of guttae (Giasson et al. 2007).

Cornea guttae are most known for their association with Fuchs dystrophy, but are not specific to the disease. However, guttae can also be seen in posterior polymorphous corneal dystrophy (PPCD), macular corneal dystrophy, and interstitial keratitis (Giasson et al. 2007; Weisenthal and Streeten 2011). There also are corneal pseudoguttae, which appear transiently during underlying trauma, infection, or inflammation (Weisenthal and Streeten 2011).

Guttae occur centrally. In this central region, the median surface area and number of guttae are the largest (Giasson et al. 2007). As the disease progresses, the guttae will appear centrally, but also spread to the periphery. Guttae of diseases like Fuchs dystrophy can often be confused with

Hassal-Henle warts. Hassal-Henle warts are degenerative changes seen in the periphery of normal adult corneas. That is in contrast to corneal guttata, which appears more centrally. Like corneal guttae seen in Fuchs dystrophy, Hassal-Henle warts are also found in the Descemet's membrane. Hassal-Henle warts do not have an association with endothelial cell function or corneal edema (Zoega et al. 2006).

Classification

Guttae are not classified, but the presence of guttae is important to the classification of the pathology they appear with. Cornea guttae are first seen in stage 1 of Fuchs dystrophy and are one of the earliest signs detectable on slit lamp examination. They often appear before symptoms occur. This early sign is important as corneal guttae represent corneal pathology and lowered endothelial cell function.

It is the presence of corneal guttae that is important in the evaluation of surgery. Ten years post cataract surgery, there is a rate of endothelial cell loss that is nearly 3 times greater for those with guttae preoperatively (Giasson et al. 2007). This lowered endothelial cell count can lead to cornea decompensation after cataract or other procedures that may damage the cornea. The risk for postoperative degeneration is greatest in those patients with thickened corneal stroma greater than 640 640 µm mu;m and with the presence of guttae (Vanmeter et al. 2013). Guttae are also important not only in the patient's eye but also in donor corneas. Interestingly, there is no difference in survival time of donor corneas with isolated guttae, but donor corneas with grouped guttae have a decreased survival time (Giasson et al. 2007).

Cross-References

- ▶ Fuchs Dystrophy
- ▶ Interstitial Keratitis
- ▶ Peripheral Corneal Guttata (Hassall-Henle Bodies/Warts)
- ▶ Posterior Polymorphous Corneal Dystrophy

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Corneal Inflammation

▶ Keratitis

Corneal Intraepithelial Neoplasia

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Definition

An abnormal cellular growth process within the epithelial layer of the cornea, characterized by changes that range from localized neoplastic proliferation to carcinoma in situ. Within the lesion, various histopathological abnormalities including but not limited to cellular pleomorphism, increase in mitotic figures, decrease in desmosomal attachments, loss of hemidesmosomes, and suprabasal mitoses can be seen (Waring et al. 1984).

References

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Corneal Keloid

▶ Keloids: Corneal and Congenital

Corneal Laceration

▶ Corneoscleral Laceration

Corneal Limbus

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Definition

The grayish-appearing circular structure located at the transition between the cornea and the sclera.

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Corneal Lipid Degeneration

▶ Lipid Keratopathy

Corneal Mapping

▶ Computerized Corneal Topography

Corneal Melting

▶ Keratolysis (Corneal Melting), Marginal, Systemic Immune-Mediated Disease

Corneal Micropuncture

▶ Stromal Micropuncture, for Recurrent Corneal Erosions

Corneal Necrosis

▶ Necrotizing Keratitis

Corneal Neovascularization

▶ Micropannus
▶ Pannus/Micropannus

Corneal Patching

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Synonym

Eye patch; Ocular pressure patch

Definition

Corneal patching refers to closing the eyelids and putting a pressure patch on the eye. It can be done unilaterally or bilaterally according to the rational for corneal patching. Before corneal patching, it is imperative that there not be any intracorneal foreign bodies.

Overview

Corneal patching is one of the methods used to treat corneal abrasions, either after trauma or in spontaneous cases due to dry eye, recurrent erosion, or neurotrophic conditions. Patching can be used in patients with seven nerve palsy or other causes of corneal exposure, both as prophylaxis and treatment of corneal epithelial injury.

Generally, after 24 h of corneal patching, healthy corneal epithelium will be renewed and the signs and symptoms of the patient related to the abrasion will improve (Fraser 2010).

Advantages and Disadvantages

Patching an eye following a corneal abrasion improves healing and also provides pain relief. Reepithelialization is associated with decreased risk of superimposed infection. Corneal patching may be more effective for large abrasions as smaller abrasions may promptly resolve with less occlusive treatment. Some abrasions may benefit from patching beyond 24 h; however, close follow-up must be maintained, and repatching should only occur after a slit-lamp examination to ensure improvement of the abrasion and the absence of infection.

Caution must be exercised in cases of trauma and contact lens wear, since patching may promote infection. If there is any question of exposure to vegetative material, corneal patching should be avoided. A further consideration is that patching abolished binocular vision, although in the context of a painful abrasion, is likely less of an issue.

Some ophthalmic surgeons prefer to patch the eye for 1 day before using topical medications after intraocular surgeries (Turner and Rabiu 2006; Flynn et al. 1998).

Outcome

The most important outcome of corneal patching is acceleration of epithelial healing, which is associated with decreased pain, increased vision, and decreased rates of injection (Flynn et al. 1998; Wilson and Last 2004).

Indications (Skuta et al. 2010–2011)

The most common indications of corneal patching are:

1. Large corneal abrasions especially due to trauma
2. Persistent epithelial defects
3. Early postoperative treatment after intraocular surgeries
4. Dellen
5. Neurotrophic lesions
6. UV keratitis

Contraindications

Whenever we are suspicious to the presence of infection or the cause of abrasion increases the risk for infectious keratitis, corneal patching should not be done. The contraindications are:

1. The presence of any sign of globe rupture
2. The presence of infiltration in the cornea
3. The presence of corneal foreign body (the corneal foreign body should be removed before patching to diminish the risk of infection)
4. Corneal abrasions that are made by contact lens (before doing corneal patching take the history of contact lens wear)
5. Corneal abrasions due to vegetative injuries (high risk for fungal infection)

Technique

1. Apply topical medications, such as cycloplegic agent and antibiotics.
2. Apply with moderate pressure one to two eyepads on the eye and affix with tape.

Caution the patient on limiting activities, including driving, and stress the importance of prompt follow-up within 24 h.

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Corneal Pigmentary Lines

► Striate Melanokeratosis

Corneal Pigmentations

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Definition

Corneal pigmentation refers to discoloration of the cornea at any of its layers.

Etiology

Pigmentations of the cornea may occur with or without ocular or systemic disease (Biswell 2011). Multiple different forms of corneal pigmentation may be encountered; the most common etiologies include local or systemic exposure to metals and medications. Deposition may occur anteriorly from the tear film, peripherally through vasculature (in arcus), or posteriorly (through the aqueous) (Naumann and Apple 1986; Khurana 2007; Biswell 2011).

Occurrence

Iron deposition: iron deposition in the cornea may occur in significant quantity to become clinically visible. This generally involves epithelial uptake of iron from the tear film and therefore correlates with lid position and tear film stasis on the ocular surface (Khurana 2007; Biswell 2011).

The *Hudson-Stahli line* is a horizontal line of deposited iron in the corneal epithelium at the junction of the upper two-thirds and the lower one-third of the cornea. This location corresponds to the line of lid closure. The Hudson-Stahli lines are a normal variant with age (Naumann and Apple 1986; Biswell 2011).

Ferry's line is iron deposition in the corneal epithelium adjacent to a filtering bleb (Khurana 2007; Biswell 2011).

Fleischer's ring is iron deposition in the corneal epithelium surrounding the base of the cone in keratoconus (Khurana 2007; Biswell 2011).

Stocker's line is iron deposition in the corneal epithelium sometimes seen anterior to the advancing head of a pterygium (Naumann and Apple 1986; Biswell 2011).

Siderosis occurs from a foreign body iron deposition in the cornea, mostly in the stroma. Siderosis bulbi refers to degenerative changes produced by an iron foreign body. Siderosis bulbi usually occurs after 2 months to 2 years of foreign body deposition (Khurana 2007).

Coat's white ring is an iron deposit in Bowman's layer associated with a previous corneal foreign body (Khurana 2007).

Copper deposition: Copper ions can become deposited under membranous structures of the eye. Unlike iron ions, copper ions do not enter into chemical combination with the proteins of the cells and therefore do not produce degenerative changes. *Chalcosis* refers to the changes produced by copper in the eye (Khurana 2007).

The *Kayser-Fleischer ring* is a golden brown ring of copper deposition under peripheral parts of the Descemet membrane in the cornea. They are usually 1–3 mm in diameter and located just inside the limbus. In exceptional cases, there is a second ring. The Kayser-Fleischer rings are almost always caused by Wilson's disease (hepatolenticular degeneration); however, they have been described in patients with chronic liver disease not due to Wilson's disease. These rings do not cause any visual problems. The intensity of pigmentation caused by the Kayser-Fleischer rings can be reduced by treatment of the abnormal copper metabolism hallmarking Wilson's disease (Khurana 2007; Biswell 2011).

Blood staining of the cornea: Blood staining occurs occasionally as a complication of hyphema or secondary to raised intraocular pressure. The cornea becomes reddish brown or greenish in color. The corneal staining is due to hemosiderin within the corneal stroma. Vision is decreased, and the cornea clears very slowly from the periphery toward the center. In most cases the cornea gradually clears in 1–2 years (Khurana 2007; Biswell 2011).

Melanin deposition: Changes in the iris can lead to melanin from the iris pigment epithelium to be released into the anterior chamber and aqueous fluid. The melanin can deposit on the posterior surface of the cornea, anterior surface of the iris, the trabecular meshwork and the lens capsule (Khurana 2007).

Krukenberg's spindle is a vertical ellipse of melanin deposited on the corneal endothelium. It is seen in patients with pigment dispersion syndrome. This syndrome is characterized by fine particles of brown uveal pigment which have dispersed from the iris and associated structures into the aqueous humor. The spindle can be seen grossly in severe cases but is best observed with a slit lamp. Pigmentary glaucoma, a type of secondary open-angle glaucoma, can occur from the pigment particles clogging the trabecular meshwork and increasing intraocular pressure. Therefore, patients presenting with Krukenberg's spindle should receive an investigative examination for glaucoma. Visual acuity is only slightly affected, and progression is very slow. This condition typically appears in young myopic males. The exact mechanism of pigment shedding is unknown (Naumann and Apple 1986; Khurana 2007; Biswell 2011).

Ochronosis is a melanin-like pigmentation of the peripheral cornea caused by alkaptonuria (Khurana 2007).

Lipid deposition: Lipids can leak out of limbal capillaries and deposit in the cornea. The deposits are composed of extracellular cholesterol, cholesterol esters, phospholipids and triglycerides (Naumann and Apple 1986).

Arcus senilis are annular gray-white opacities consisting of lipid deposits within the corneal stroma located near the cornea periphery. The arcus, approximately 1–1.5 mm in width, is separated from the limbic edge by the lucid interval of Vogt. This is an age-related change occurring bilaterally in 60% of patients between 40 and 60 years of age and in nearly all patients over the age of 80. Arcus senilis does not require treatment and does not affect vision. When found in individuals under the age of 50, the term used is arcus juvenilis and is possibly a sign of abnormal lipid metabolism and increased LDL production. The lipid deposits will initially form as arcs at the superior and inferior peripheries of the cornea. The arcs may progress with accumulation of lipid deposits to form a complete ring (Naumann and Apple 1986; Khurana 2007; Biswell 2011).

Silver deposition: Discoloration due to inappropriate exposure to chemical compounds containing silver is termed *argyrosis* and can appear throughout the body including the cornea. Discoloration of the cornea is caused by deposition of silver in the Descemet membrane. Peripheral and diffuse corneal depositions have been

documented. Central corneal involvement occurs with longer exposure. Silver deposits cause a blue-gray discoloration (Khurana 2007).

Gold deposition: Gold treatment for arthritis may lead to corneal gold deposition, termed *chrysiasis*. These are gold to violet in color and generally do not affect vision. Deposits are found in the anterior portion of the cornea (epithelium and anterior stroma) with lower cumulative doses of gold (1–2 g), but higher doses result in depositions in the posterior cornea (the Descemet membrane and the posterior stroma) (Khurana 2007).

Adrenochrome deposition: Oxidized epinephrine can be deposited on the conjunctiva or in Bowman's layer of the cornea in patients using topical epinephrine compounds. Depositions cause a dark discoloration (Khurana 2007).

Classification

Location	Substance	Location	Appearance
Anterior cornea	Iron	Epithelium	Brown discoloration, often distributed inferiorly and associated with tear film
	Cornea verticillata (amiodarone, chloroquine, hydroxychloroquine, indomethacin, phenothiazines)	Basal layer of epithelium (substances bind to cellular lipids)	Whorl-like pattern of golden brown or gray deposits, often seen inferiorly
	Adrenochrome deposits (epinephrine, tetracycline, or minocycline)	Bowman's layer	Dark discoloration
	Fluoroquinolone deposits (often ciprofloxacin)	Subepithelial	White crystals in an epithelial defect
Central cornea	Lipid (arcus)	Stroma	Peripheral whitening
	Iron	Stroma	Iron foreign body deposition directly in the stroma may result in a rust ring
Posterior cornea	Hemosiderin	Posterior stroma	Golden brown discoloration
	Silver	Descemet membrane	Blue-gray discoloration
	Copper	Descemet membrane	Kayser-Fleischer ring
	Gold	Descemet membrane or posterior stroma in high doses (lower doses deposit in the epithelium and anterior stroma)	Gold to violet discoloration
	Melanin (Krukenberg's spindle)	Endothelium	Scattered brown pigment on corneal endothelium may be confused for guttae

Cross-References

- Chloroquine Toxicity, Cornea Verticillata
- Chlorpromazine, Cornea Verticillata
- Chrysiasis, Corneal Pigmentation
- Kayser-Fleischer Ring
- Khodadoust Line
- Krukenberg Spindles
- Siderosis: Signs and Symptoms

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Corneal Protein Fibrils

► Corneal Collagen

Corneal Stromal Haze

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Definition

The term "haze" commonly describes a condition of mild anterior corneal stromal opacification which occurs as part of the normal wound healing response after keratorefractive procedures, especially excimer laser surface ablation.

Histology

Haze occurs as a wound healing response to the corneal epithelial and stromal injury caused by excimer laser ablation. The disruption of the epithelial basement membrane leads to apoptosis and necrosis of the stromal corneal cells. This causes activation and centripetal migration of keratocytes which transform into activated fibroblasts which then further transform into myofibroblasts.

Immunohistochemistry

In the development of haze, the distribution of collagens in the cornea changes with an increase of fibrillar type IV collagen. An increased expression of the extracellular matrix by the activated keratocytes is observed. By blocking of TGF-b, the formation of haze has been inhibited in animal experiments.

Confocal Microscopy

Confocal microscopic findings in corneas after corneal surface ablation include an increased light backscattering which is caused predominantly by a higher density of activated keratocytes. (Moller-Pedersen et al. 2000)

Molecular Diagnostics

No publications found.

Differential Diagnosis

Differential diagnoses include corneal scarring after inflammation or trauma and corneal dystrophies.

Cross-References

► Corneal Collagen
► Confocal Microscopy
► Cornea
► Photorefractive Keratectomy (PRK)

References

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Corneal Tattoo

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Definition

Corneal tattooing refers to the delivery of pigment into the corneal stroma to improve the cosmetic appearance of disfiguring scars or reduce the glare and visual distortion in patients with large iridectomies, traumatic loss of iris, or congenital

iris colobomas. Tattooing can be especially helpful for patients in whom reconstructive surgical procedures will not result in functional improvement or for those who are unable to tolerate a printed contact lens or bulbar shell.

Impregnation techniques have been used for nearly 2000 years, in which the dye is delivered with the use of multiple punctures perpendicular to the corneal surface. Newer techniques include (a) the application of a platinum ion solution to the cornea, which when reacted with a second agent forms a dark black precipitate in the cornea and (b) a dermatography-like manner of tattooing, which employs punctures parallel to the corneal surface with a conventional spatula needle. Most recently, the success of femtosecond-assisted corneal tattooing has been reported. With this technique, an anterior lamellar corneal free flap created using a femtosecond laser is removed and incubated in a commercially available black tattoo pigment and then repositioned on the residual corneal bed and covered with a bandage contact lens. Alternatively, a hinged flap may be used instead, with the direct injection of dye into the lamellar stromal bed before replacement of the flap. Determination of the long-term safety and success of these newer techniques is ongoing.

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Corneal Thickness

► Central Corneal Thickness

Corneal Tomography

► Computerized Corneal Topography

C

Corneal Topography

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Synonyms

Computerized videokeratography

Definition

Method for measurement, visualization, and analysis of corneal curvature across the entire cornea.

Purpose

Corneal topography is used to quantify and visualize the curvature of the corneal first surface (Scheimpflug-based devices also image the posterior surface) and to reveal astigmatism and corneal irregularities. It ranges between anatomical imaging and functional exam.

Principle

The use of powerful personal computers, high-resolution video cameras, and modern image analysis software allowed a merge of qualitative keratoscopy and quantitative keratometry: The reflection of a pattern of concentric circles (Placido disk) on the cornea is captured by a digital camera. A computer calculates corneal curvature at each corneal point based on the distance of the mires in the corneal reflection image. On a color contour map, curvature is plotted as a function of location, hence the term "corneal topography."

Placido-based corneal topographers were those first constructed and are still the most widespread

used topography devices. Scheimpflug-based topographers produce optical sections of the cornea, enabling the measurement of both anterior and posterior corneal surface. From raw images, corneal height, curvature, refractive power as well maps of corneal thickness can be calculated. Some manufacturers have equipped their Scheimpflug topographers with a Placido disk for anterior surface imaging, while others rely on the improved resolution of new generation CCD cameras and offer a Scheimpflug-only solution.

Indication

Diagnostics of corneal diseases (e.g., keratoconus, scars), contact lens fitting, preparation, and follow-up of refractive surgical procedures.

Contraindication

Corneal topography is noninvasive. There are no contraindications.

Advantage/Disadvantage

Corneal topographic exams are captured easily without pupil dilation and without discomfort for the patient. Apart from corneal back surface imaging, rotating Scheimpflug cameras have the advantage of high-density imaging of the central cornea, because this region is imaged in each frame. Correspondingly, the disadvantage of Placido topographers is the sparing of the corneal center because of the location of the camera front lens. For measurement of the whole optical properties of the eye, a wavefront sensor (aberrometer) is needed.

Cross-References

- ▶ Implantable Contact Lens
- ▶ Keratoconus
- ▶ Photokeratoscopy
- ▶ Refractive Surgery
- ▶ Wavefront Sensing

References

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Corneal Ulceration

- ▶ Ulcerative Keratitis Disease

Corneal Ulcers

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Definition

A corneal ulcer is a local corneal inflammation that presents with an opacity in the cornea, adjacent conjunctival redness, pain, and possible discharge. The presence of an opacity within the cornea differentiates ulcers from abrasions. Corneal ulcers require emergent treatment as loss of vision can occur very rapidly.

Corneal Vascularization

- ▶ Micropannus
- ▶ Pannus/Micropannus

Corneal Verticillata

- ▶ Striate Melanokeratosis

Corneal White Dot

- ▶ Coats' White Ring

Corneocytes

► Keratinocytes: Overview

Corneo-Fundal Potential, The

► Electrooculogram

Corneoretinal Dystrophy, Bietti's Crystalline

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Synonyms

Bietti's corneoretinal crystalline dystrophy; Bietti's crystalline dystrophy; Bietti's tapetoretinal degeneration with marginal corneal dystrophy

Definition

A rare hereditary condition marked by concurrent crystalline retinopathy, progressive pigmentary retinopathy, and marginal corneal dystrophy.

Etiology

Bietti's crystalline dystrophy (BCD) is inherited in an autosomal recessive fashion; 39 mutations in the cytochrome P450 4V2 gene have been identified. CYP450V2 codes for a fatty acid omega hydroxylase thought to be active in fatty acid metabolism (Rossi et al. 2013); studies suggest that dyslipidemia may occur in concert with BCD in nearly half of affected patients. Thus, BCD may be caused by a global abnormality of lipid metabolism.

Clinical Presentation

Patients present most commonly in the second or third decades of life with decreased central acuity, progressive nyctalopia, and paracentral scotoma.

Anterior segment involvement may manifest as refractile corneal crystals in the superficial corneal stroma at and about the limbus as well as the conjunctiva. Posterior segment involvement is characterized by yellow or white intraretinal refractile crystals superimposed on diffuse retinal pigment epithelium (RPE) atrophy, pigmentary clumping, and atrophy of the choriocapillaris. Vascular attenuation and optic disc pallor too may be present in advanced disease. These findings are progressive (Mataftsi et al. 2004; Sahu and Rawoof 2002).

Diagnosis

Electroretinogram (ERG) may reveal subnormal photopic and scotopic responses. Electrooculogram (EOG) too may reveal a subnormal response. Perimetry may unmask scotomata corresponding to areas of chorioretinal atrophy.

Pathology

Pathology finds crystalline deposits and lipid inclusions in choroidal fibroblasts, corneal keratocytes, conjunctival and cutaneous fibroblasts, as well as in lymphocytes in the peripheral circulation (Yanoff and Fine 1996).

Differential Diagnosis

Clinical presentation is similar to but must be differentiated from fundus albipunctatus, retinitis pigmentosa albescens, oxalosis, cystinosis,

canthaxantin or tamoxifen retinopathy, talc retinopathy, Sjogren-Larsson syndrome, idiopathic juxtafoveal retinal telangiectasia, and gyrate atrophy.

Prophylaxis

No effective prophylaxis is recognized as yet.

Therapy

No effective treatment is recognized as yet.

Prognosis

Affected patients typically progress to legal blindness by fifth or sixth decades of life.

Epidemiology

Patients are most commonly of East Asian descent, particularly of Japanese or Chinese ancestry. BCD has been estimated to comprise 3% of nonsyndromic retinitis pigmentosa cases.

Cross-References

- ▶ Fundus Albipunctatus
- ▶ Retinitis Punctata Albescens

References

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Corneoscleral Laceration

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Synonyms

Corneal laceration; Open globe; Ruptured globe; Scleral laceration

Definition

A partial- or full-thickness injury to the cornea and sclera, extending through the limbus. A - partial-thickness injury does not penetrate the globe, whereas a full-thickness injury results in a ruptured globe.

Etiology

Corneoscleral laceration refers to a penetrating injury by a sharp object and/or projectile. This is not to be confused with a corneoscleral rupture which is caused by blunt trauma inducing defects at the areas of weakness of the globe (the equator and behind the rectus muscles). Lacerations are further described as penetrating vs. perforating:

Penetrating: entry wound without an exit wound
Perforating: entry and exit wound

Clinical Presentation

Any ocular trauma should raise a concern for a corneoscleral laceration. Injuries that include

high-speed projectiles such as metal grinding or wood chipping should be thoroughly investigated before ruling out a ruptured globe. The patient may exhibit a foreign body sensation, tearing, and pain, though the lack of these findings does not rule out a corneoscleral laceration. An intraocular foreign body should always be considered in conjunction.

The following signs are indicative of a ruptured globe:

1. Prolapsed uveal tissue
2. Seidel positive (application of fluorescein shows clear aqueous flowing out of the wound)
3. Vitreal prolapse
4. Visualized intraocular foreign body or intraocular foreign body on radiography

Signs suggestive of a ruptured globe include:

1. Decrease in vision following trauma
2. New afferent papillary defect following trauma
3. Peaked pupil toward the site of injury, often called a teardrop pupil
4. Low intraocular pressure
5. Shallow anterior chamber
6. 360 hemorrhagic chemosis
7. Focal lens defect
8. Full-thickness eyelid laceration

Diagnosis

Patients with corneoscleral lacerations often have other injuries. First and foremost any life-threatening condition should be appropriately treated. Once the patient is stable, the evaluation of a corneoscleral injury can begin. The importance of a careful history cannot be overstated. Among other questions, details regarding the mechanism of injury are vital. These include but are not limited to:

1. High-speed projectile
2. Material of object (i.e., metal, plant matter, soil contamination, wood, etc.)
3. Previous treatment including those undertaken prior to arrival in a situation requiring transfer of a patient
4. Use of eye protection during event

Changes in vision and visual acuity prior to the trauma are vital details affecting management and prognostication. Presurgical questioning such as the time of last meal, allergies, and past ocular, medical, and surgical history is important to elicit early should the patient require emergent repair in the operating room. Past ocular history includes previous surgeries, the presence of refractive errors, the use of ocular medications, and other ocular diseases. Medical history includes diagnoses, medications, vaccination history including tetanus, and further questions by the anesthesia/medical clearance team in the setting of a presurgical anesthesia evaluation. Determining the capacity for medical decision-making and identifying the correct person to consent (especially in the case of a minor or those unable to consent for themselves) should not be overlooked.

A physical and ocular exam follows the history. Document vital signs early at presentation, especially cases with multiple bodily injuries and continue to observe should lifesaving interventions become necessary.

Evidence of extrusion of any intraocular material including uvea, lens, vitreous, or aqueous fluid is diagnostic for a full-thickness laceration.

After instillation of topical anesthetic, a gentle examination of wounds suspicious for laceration is undertaken. During this exam care is taken to avoid pressure on the globe should extrusion of intraocular occur. Pain control and anti-emesis medication is often given prior to exam in an effort to prevent clenching and Valsalva, respectively, which also carry risk of extrusion.

Fluorescein is used for Seidel testing by applying directly to the concerned area. During blue light examination, any flow of clear fluid out of the wound is indicative of a positive test and globe rupture. Gentle digital pressure may be applied to the globe if a self-sealing wound is suspected.

Hemorrhagic chemosis, particularly 360°, may hide a laceration. This should be explored, usually with topical anesthetic and cotton tip applicators, though exploration in the OR is also warranted when a rupture cannot be ruled out.

A CT scan should be obtained to rule out intraocular foreign bodies. MRI is contraindicated unless the physician is sure no metallic objects are involved.

Differential Diagnosis

Corneal abrasion
Scleromalacia perforans

Prophylaxis

A shield should be placed over the eye after diagnosing a laceration. The patient should be kept NPO in the case of surgical management. All procedure that involves pressure on the globe should be avoided.

Broad-spectrum intravenous antibiotics with coverage for *Bacillus* species should be given. These include fluoroquinolones, clindamycin, and vancomycin. Pain control and anti-emetics should be administered to prevent an increase in intraocular pressure and possible extrusion of intraocular contents.

Tetanus vaccine should be given when the patient's tetanus status is not current or unknown.

Therapy

If a partial-thickness laceration is found, then topical antibiotic prophylaxis and optional cycloplegia for comfort can be utilized. In severe cases a bandage contact lens may be placed to avoid further disruption.

If the wound is small with no tissue compromise, then nonsurgical management can be considered. The anterior chamber should be carefully inspected and remain well formed. Management includes antibiotics and frequent follow-up with anterior chamber and wound assessment. A bandage contact lens is also considered when a slow leak is present along with aqueous suppressants. Unresolving leaks and/or lacerations should be surgically closed after 48–72 h of observation.

The primary goal of surgical intervention is to restore the globe integrity with watertight closure and is usually performed within 24 h of presentation when the above conditions are not met. The secondary goal is to restore as much vision as possible. Globe repair is accomplished first followed by adnexal repair of injuries without the usage of muscle retraction sutures. The basic clinical and science course outlines 11 basic steps for closure:

- General anesthesia
- Excision of anteriorly prolapsed vitreous, lens fragments, and corneal foreign bodes
- Repositioning of anteriorly prolapsed uvea, retina
- Closure of corneal component of laceration at limbus, landmarks
- Completion of watertight corneal closure [with] 10-0 nylon
- Peritomy as necessary for exposure of scleral component
- Stepwise excision of posteriorly prolapsed vitreous
- Stepwise repositioning of posteriorly prolapsed uvea, retina
- Stepwise closure of scleral component [with] 9-0 nylon or 8-0 silk
- Conjunctival closure
- Subconjunctival antibiotics and corticosteroids

The patient is assessed for the risk of sympathetic ophthalmia when an NLP eye presents. In these situations enucleation should be considered. Primary enucleation should only occur when tissue injury is completely devastating without a chance of restoration of anatomy and the patient is mentally prepared for this outcome. Twelve to 14 days is generally accepted as the window period prior to the onset of sympathetic ophthalmia though cases have been presented with earlier manifestation. Therefore enucleation can wait to be performed outside the directly emergent setting in order for further assessment.

Postoperative treatments to prevent endophthalmitis and decrease inflammation are also indicated.

Prognosis

Prognosis varies greatly based on the extent of injury and the presence of other factors such as tissue loss, traumatic cataract formation, and stromal scarring. Initial visual acuity, the presence of afferent papillary defect, posterior wound location, and associated lid lacerations are predictive of worse outcomes in the repair of ruptured globes. Visual acuity at presentation is the most reliable predictor of final visual outcome.

Epidemiology

Young males have shown a higher incidence of corneoscleral lacerations.

Cross-References

- ▶ Eyelid Trauma
- ▶ Penetrating Injuries
- ▶ Subconjunctival Hemorrhage

Further Reading

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Cornified Keratinocytes

- ▶ Keratinocytes: Overview

Coronal Scalp Flap, for Anterior Orbitotomy

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The Aesthetic Institute of West Florida, Largo, FL, USA

C

Definition

A surgical procedure elevating a coronal flap to obtain broad access and exposure to the anterior and lateral orbit and surrounding areas.

Indications

This technique is most often used for lateral bony or intraconal lesions to allow broad exposure. It also provides direct and broad exposures for patients who have multiple orbital fractures, including the superior orbital rim or bone, as well as multiple other facial fractures (Nerad 2001; Levine 2003; Paolini et al. 2006).

Contraindication

Contraindication for patients unable to medically tolerate surgery or anesthesia or for those with more localized lesions that may be accessed with a more limited technique.

Techniques and Principles

Under general anesthesia, a coronal flap is elevated beveling the incision to maintain hair follicles. It is then carried inferiorly either in a subperiosteal or subfascial plane taking care to avoid damage to the frontal branch of the facial nerve. The area of interest is exposed as necessary for facial fracture repair or lateral orbitotomy (Nerad 2001; Levine 2003; Paolini et al. 2006).

Outcome

Broad exposure for lesion removal or fracture repair of the anterior orbit. Excellent aesthetic closure with incision hidden in hair, avoiding any external skin incisions and risk of scarring.

Complications

Risks of a coronal scalp flap anterior orbitotomy include risks associated with anesthesia, bleeding, pain, infection, scarring, swelling, loss of vision, damage to adjacent structures, parasthesia diplopia, alopecia, and need for additional procedures (Nerad 2001; Levine 2003; Paolini et al. 2006).

Cross-References

- ▶ Anterior Orbitotomy
- ▶ Lateral Orbitotomy
- ▶ Orbit, Inflammation of

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Cortical Cleaving Hydrodissection

- ▶ Hydrodissection

Corticoid

- ▶ Corticosteroids

Corticosteroid

- ▶ Corticosteroids

Corticosteroids

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Synonyms

Adrenal cortical steroid; Corticoid; Corticosteroid; Steroid hormone

Definition

Corticosteroids, endogenous hormones produced by the adrenal cortex, are divided into glucocorticoids (GCs) and mineralocorticoids (MCs). Synthetic or semisynthetic GCs have been produced to enhance the anti-inflammatory properties of GCs while reducing their mineralocorticoid activity for therapeutic purposes.

Cortisol is the more abundant circulating GC in human. The synthesis of GCs is regulated by the hypothalamic–pituitary–adrenal axis. The corticotrophin-releasing hormone (CRH) is produced by the hypothalamus and leads to adrenocorticotropic hormone (ACTH) secretion by the anterior pituitary gland, which in turn regulates the GC secretion by the adrenal cortex. Cortisol has a negative feedback on ACTH and CRH production.

Aldosterone is the most potent MC in humans. The secretion of MCs is regulated by the

renin–angiotensin system and blood potassium levels to control body fluid volume and blood pressure.

Among synthetic corticosteroids, the most commonly used for their therapeutic action are cortisone, prednisolone, prednisone, methylprednisolone, dexamethasone, triamcinolone, betamethasone, and fludrocortisone. One of the pharmacological features distinguishing corticosteroids from one another is their relative GC versus MC potency (Table 1). Potency of GCs has been evaluated on the basis of their vasoconstrictor effects (McKenzie test) and on their ability to reduce in vitro inflammatory cell activation. Their mineralocorticoid potency was mostly based on their ability to slow ACTH production or to raise the systemic blood pressure. No classification system has ever been designed for the specific ocular use of GCs.

GCs have pleiotropic effects on development, metabolism, cognitive function, and homeostasis. As potent anti-inflammatory, immunosuppressive, and anti-allergic agents, synthetic GCs have been widely employed for decades in the clinical setting.

In contrast, MCs are a key regulator of the balance of fluids and electrolytes. Pharmacologically, inhibition of the MC pathway at different levels aims at lowering blood pressure and controlling heart and vascular remodeling processes.

Mechanisms of Action

Corticosteroids, being transcription factors, act mainly through classical genomic regulation mechanisms, which are also largely responsible for their side effects. In addition to these genomic effects, corticosteroids also act via rapid non-genomic mechanisms either through binding to their receptors or independently. Most of the genomic effects are indeed mediated by the GC receptor (GR) and MC receptor (MR) (Fig. 1).

Corticosteroids, Table 1 Relative gluco- and mineralocorticoid potency to hydrocortisone of commonly used corticosteroids

Preparation	Glucocorticoid[a]	Mineralocorticoid
Hydrocortisone (cortisol)	1	1
Cortisone	0.8	0.8
Prednisolone	4	0.8
Prednisone	4	0.8
Methylprednisolone	5	0.5
Triamcinolone	5	0
Dexamethasone	25	0
Betamethasone	25	0
Fludrocortisone	10	125

[a]Anti-inflammatory potency

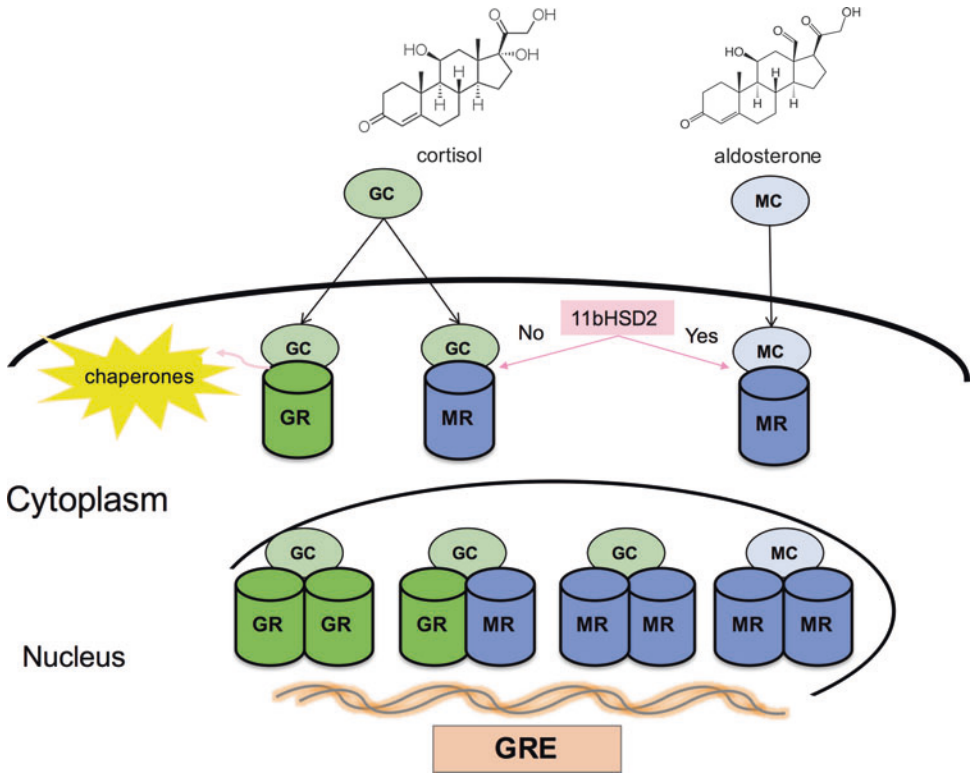
Mineralocorticoid Receptor (MR)

The MR has two ligands, aldosterone and cortisol, which bind to the MR with the same affinity. Since cortisol levels largely prevail over aldosterone levels in the plasma (cortisol is around 1000 times more concentrated than aldosterone), MR is occupied by cortisol unless the 11-ß-hydroxysteroid dehydrogenase type II (11bHSD2), protecting the MR from being occupied by cortisol, is expressed. The 11bHSD2 pre-receptoral enzyme metabolizes cortisol to cortisone which cannot bind to the MR with similar affinity. On the other hand, the 11BHSD type I enzyme exerts the reverse conversion from cortisone to cortisol. There is a balance between both enzymes that control the availability of cortisol to bind to its receptor. Thus, only in tissues where the 11bHSD2 is present, aldosterone can activate the MR, such as the kidney which is the classical mineralo-sensitive organ. Several non-epithelial MR-expressing tissues, including the heart, adipocytes, and macrophages, do not express 11bHSD2, and therefore, the MR is activated by cortisol in these tissues.

Glucocorticoid Receptor (GR)

Cortisol binds with high affinity to the GR, which leads to the dissociation of molecular chaperones from the GR. The cortisol–GR complex moves to the nucleus, where it binds as a homodimer to specific sequences of DNA called glucocorticoid-responsive elements (GREs). The resulting complex recruits either coactivator or corepressor proteins that modify the access to chromatin, thereby facilitating or inhibiting the transcription of target genes.

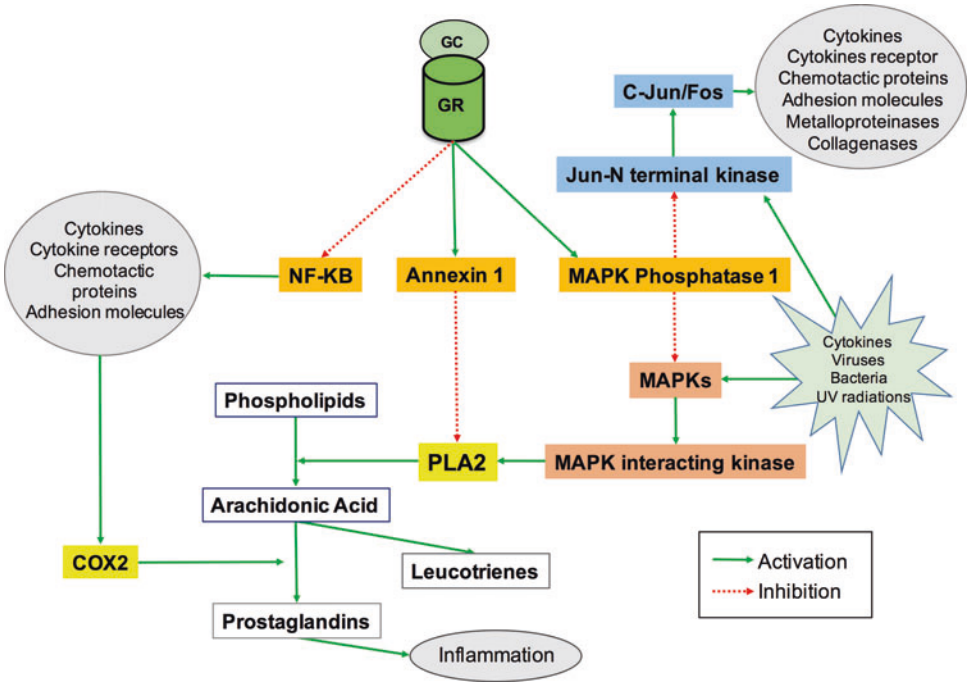
The anti-inflammatory effect of GCs relies on negative regulation of pro-inflammatory mediators and the positive regulation of anti-inflammatory



Corticosteroids, Fig. 1 Genomic mechanisms of action of corticosteroids. Glucocorticoids (*GC*s) bind glucocorticoid receptor (*GR*) or mineralocorticoid receptor (*MR*), which leads to the dissociation of molecular chaperones from the receptor. In cells where the enzyme 11ß-hydroxysteroid dehydrogenase type II (*11bHSD2*) is present, aldosterone can bind the MR. The cortisol–GR complex is displaced to the nucleus, where it binds as a homodimer to DNA sequences called glucocorticoid-responsive elements (*GRE*s)

factors. GCs inhibit prostaglandin and cytokines via three main mechanisms: activation of the transcription of annexin I and mitogen-activated protein kinase phosphatase 1 (MAPK phosphatase 1) and inhibition of nuclear factor-kB (NF-kB) (Fig. 2). First, GCs induce the transcription of annexin I (also called lipocortin-1), which by inhibiting cytosolic phospholipase A2-alpha (PLA2) blocks the release of arachidonic acid and its conversion to eicosanoid as prostaglandins, thromboxanes, prostacyclins, and leukotrienes. GCs induce the transcription of MAPK phosphatase 1 which inactivates Jun N-terminal kinase (JNK pathway), inhibiting c-Jun-mediated transcription that upregulates cytokines as tumor necrosis factor-alpha (TNF-alpha) and enzymes as inducible nitric oxide synthase (iNOS), metalloproteinases, and collagenases, among others. MAPK phosphatase 1 also inactivates all members of the MAPK proteins and thereby PLA2 activity. Third, the cortisol–glucocorticoid receptor complex exerts a strong negative regulation of cytokine expression through its interaction with other transcription factors, such as NF-kB. Indeed, GC inhibits the NF-kB pathway, which is responsible for the transcription of cytokines, chemokines, cell adhesion molecules, complement factors, and cyclooxygenase-2 (COX-2), an essential enzyme for prostaglandin production.

There are two isoforms of the GR: alpha and beta. The alpha isoform is the classical active isoform that binds cortisol, DNA, and other transcription factors and modifies the transcriptional activity of genes. GR-beta acts as a dominant



Corticosteroids, Fig. 2 Molecular events triggered by the genomic action of glucocorticoids. Glucocorticoids (*GCs*) binding to the glucocorticoid receptor (*GR*) induces the transcription of annexin I and MAPK phosphatase 1 and the repression of transcription of nuclear factor-kB (*NF-kB*). Thereby, GCs inhibit the expression of a wide range of cytokines, chemokines, cell adhesion molecules, as well as cyclooxygenase-2 (*COX-2*) and cytosolic phospholipase A2-alpha (*PLA2*), which inhibits the release of prostaglandins and leukotrienes

negative regulator of GR-alpha transcriptional activity. Higher levels of GR-beta in a cell lead to glucocorticoid resistance.

Finally, corticosteroids also exert non-genomic effects through signaling via potential membrane-associated receptors and second messengers, regulating the translation to proteins. One of these non-genomic mechanisms include the decreased stability of messenger RNAs coding for inflammatory proteins such as vascular endothelial growth factor (VEGF) and COX-2.[9] Recent evidence suggests that GCs could influence the methylation of their own genes causing epigenetic regulation of their activity.[10]

Indication

GCs are widely employed in ophthalmology because of their anti-inflammatory, anti-edematous, immunosuppressive, and anti-allergic properties. Systemic or local GCs are essential agents and may be used for the treatment of numerous ocular disorders involving all parts of the eye: conjunctivitis, episcleritis, scleritis, keratitis, anterior and posterior uveitis, retinal edema of many etiologies (uveitis, diabetes, retinal vein occlusion, postoperative), and optic neuropathies.

GCs inhibit PLA2, COX-2, NF-kB, NO synthase, and cytokines: interleukin-1 (IL-1), interleukin-6 (IL-6), TNF-alpha, and prostaglandin E2 (PGE2). GCs attenuate leukocyte recruitment, intercellular adhesion molecule 1 (ICAM-1), mRNA expression, and VEGF. In endothelial cells, GCs induce the expression of junction proteins, such as occludin and claudin-5, contributing to the blood retinal barrier restoration, and directly reduce the formation of new vessels (anti-angiostatic effect). In retinal glial Müller cells, GCs regulate the expression and

distribution of ion channels and water channels. Interestingly, dexamethasone and triamcinolone exert a specific and differential regulation of Kir4.1 (K^+ inwardly rectifying channel 4.1) and AQP4 (aquaporin 4) suggesting that the dose and type of corticosteroid may influence their anti-edematous properties. Finally, GCs protect against oxidative-stress-induced disruption of tight-junction proteins in retinal pigment epithelial cells.

Contraindications

Ocular corticosteroids are contraindicated in patients with hypersensitivity to any components of the product. Special care is recommended in patients presenting with ocular or periocular infection, glaucoma, and history of central serous chorioretinopathy.

Topical corticoids should be avoided when corneal epithelial defects, fungal keratitis, herpes keratitis, or any other uncontrolled infectious diseases of the cornea or conjunctiva are present.

When indicated to treat an ocular disorder, systemic corticosteroids should be used with caution and more so in patients with the following conditions:

- Osteoporosis or any skeletal disease
- Current or past tuberculosis
- Infections of any type (virus, bacteria, fungus, amoeba)
- Underactive or overactive thyroid
- Liver disease
- Digestive disorders
- Diabetes
- Heart disease
- Elevated blood pressure
- Elevated cholesterol
- Kidney disease or kidney stones
- Myasthenia gravis
- Systemic lupus erythematosus
- Emotional or psychiatric problems
- Skin conditions causing the skin to be thinner and bruise more easily

Use and Dosage

For each route of administration, the most frequently used GCs in ophthalmology are:

- Systemic: prednisone and methylprednisolone
- Topical: dexamethasone, prednisolone, betamethasone, fluorometholone, and loteprednol
- Periocular: dexamethasone, betamethasone, and triamcinolone acetonide
- Intravitreal: triamcinolone acetonide (1–4 mg), dexamethasone, and fluocinolone acetonide

Recently, two drug delivery systems have been developed for the sustained intravitreal release of glucocorticoids: the dexamethasone implant (0.7 mg over 4 months) and the fluocinolone acetonide insert (0.2 μg/day over 36 months). These new treatments have expanded the toolbox available for the management of macular edema secondary to a range of retinal conditions.

Adverse Reactions

Ocular Side Effects

Side effects vary with the type of corticosteroid, the route of administration, and the dose and duration of treatment.

Cataract

The mechanisms of steroid-induced cataract are not fully understood. It can develop after either ocular or systemic steroid treatment. Higher doses of GCs are more likely to provoke lens opacification. The intravitreal administration of more hydrophobic GCs seems to be more frequently implicated.

Steroid-induced posterior subcapsular cataracts exhibit three main distinctive characteristics: exclusive association with GC-activity steroids, involvement of aberrant migrating lens epithelial cells, and central posterior location. Transcriptional changes may occur in lens epithelial cells, which express the nuclear GR-alpha, affecting many cellular processes such as proliferation, differentiation, apoptosis, transmembrane transport, protein aggregation, and reactive oxygen species

activity. An imbalance in intraocular cytokines and growth factors affecting the lens homeostasis has also been suggested.

Ocular Hypertension and Glaucoma

Corticosteroid-induced ocular hypertension results from an elevated resistance to aqueous outflow and/or an increased aqueous humor production. Postulated mechanisms include microstructural changes in the trabecular meshwork, deposition of precipitated substances in the trabecular meshwork, and inhibition of trabecular phagocytosis by endothelial cells contributing to this accumulation of substances, as well as changes in gene expression and cell function. A decreased amount of GR-beta in trabecular meshwork cells has been observed in glaucomatous patients. This differential distribution of the beta-isoform of the GR may be responsible for the enhanced GC responsiveness and ocular hypertension in glaucomatous patients compared to the normal population.

Retinal Toxicity

A direct in vitro toxicity of GCs on retinal vascular endothelial cells has been observed via autophagy, caspase-dependent and caspase-independent cell death, and direct DNA damage.

Central Serous Chorioretinopathy (CSCR)

The systemic or local administration of corticosteroids (via inhalation, epidural injections, intra-articular injections, topical dermal, or periocular injections) has been associated with the triggering, prolongation, aggravation, and recurrence of CSCR.

Others

The topical administration of GCs is known to delay corneal wound healing, induce scleromalacia in at-risk eyes, favor the appearance of ptosis, and increase the risk of corneal infections.

Systemic Side Effects of Glucocorticoids

The main systemic side effects of GCs are:

- Endocrine functions: Cushing's syndrome, impaired glucose metabolism
- Cardiovascular system: dyslipidemia, hypertension (fluid retention), thrombosis, and vasculitis
- Kidney: increased sodium retention and potassium excretion
- Central nervous system: changes in behavior, cognition, memory, and mood
- Gastrointestinal tract: gastrointestinal bleeding, pancreatitis, and peptic ulcer
- Immune system: broad immunosuppression and activation of latent viruses
- Skin: delayed wound healing, erythema, hypertrichosis, perioral dermatitis, petechiae, acne, and striae
- Musculoskeletal system: muscle atrophy, osteoporosis, and retardation of longitudinal bone growth
- Reproductive system: delayed puberty, fetal growth retardation, and hypogonadism

Interactions

Several classes of drug present known interactions with systemic corticoids: anticoagulants, anticonvulsants, diabetes medication, HIV medication, certain vaccinations, and nonsteroidal anti-inflammatory drugs, among others.

These interactions are very rare with local corticosteroids, especially with topical or periocular administration, but caution should be taken since severe ocular disorders requiring corticosteroid treatment often occur in fragile patients with multiple treatments.

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Corticosteroids, Use in Ophthalmology

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Synonyms

Glucocorticoids; Mineralocorticoids; Steroids

Definition

Corticosteroids are one of two types of steroids produced by the adrenal cortex. Adrenocorticotropic hormone controls the conversion of cholesterol to steroids using cAMP as the mediator. It consists of twenty one carbon atoms and is divided into glucocorticoids and mineralocorticoids.

The natural corticosteroids are cortisol, cortisone, corticosterone, and aldosterone. Some examples of the synthetic forms include prednisone, dexamethasone, triamcinalone, bethamethasone, medrysone, and fluorometholone.

The actions of corticosteroids are both immunosuppressive and anti-inflammatory by reducing lymphocyte availability and interfering with production or function of lymphokines.

Indication

Corticosteroids are the most commonly used anti-inflammatory and immunosuppressant drugs in medicine. Treatment of postoperative inflammation is the most common use in ophthalmology.

They are also used to treat conditions of immune hyperactivity including uveitis, corneal infiltrates, allergic disorders, graft rejection, and others. Corticosteroids help prevent damage from the body's own immune response.

In addition, steroids can be used to treat infectious processes at certain points in the disease. Extreme caution must be used in these cases due to potential worsening of the infection.

Contraindications

Steroids should be used with caution in the presence of bacterial, viral, fungal, and protozoal infections. Patients with diabetes mellitus, hypertension, gastric ulcer disease, history of elevated intraocular pressure in glaucoma or associated with steroid use should be monitored closely for worsening of disease. These individuals may require adjustments in their medications to minimize or avoid permanent damage from corticosteroid treatment.

Use and Dosage

Method of drug delivery includes intramuscular, intravenous, oral, inhaled, and topical. The pharmacological characteristics of these preparations vary by absorption, metabolism, and solubility. Therefore the dosage will depend on the preparation and treatment goals. Initially it may be administered in medium or large doses to suppress inflammation. A gradual taper is necessary to avoid rebound inflammation.

Potential for toxicity can also determine the method of treatment. For example, treatment with oral prednisolone may be necessary if hepatic disease is limiting the conversion of oral prednisone to prednisolone.

Adverse Reactions

Side effects from corticosteroid use can be ocular or systemic. Ocular side effects include cataracts, ocular hypertension, glaucoma, delayed wound healing, corneal melting which could lead to corneal perforation, and secondary bacterial, viral, or fungal infections.

Systemic absorption of ocular steroids can be significant and lead to fluid and electrolyte abnormalities, hypertension, hyperglycemia, increased

susceptibility to infection, osteoporosis, myopathy, and behavioral changes.

Interactions

Individuals taking steroids should not be immunized with live vaccines. Steroids may interfere with vaccines ability to protect against the disease process. Examples of live vaccines include measles, mumps, rubella, oral polio, rotavirus, smallpox, typhoid fever, yellow fever, varicella, H1N1, and nasal flu.

Corticosteroids can also interfere with aspirin, diuretics, Coumadin, insulin, rifampin, phenytoin, and phenobarbitol.

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Crab Louse

► Phthirus Pubis (Crab/Pubic Louse), Ocular Infection

Cranial Nerve II (CN II)

► Optic Nerve (Cranial Nerve II)

Cranial Nerve III

► Cranial Nerve III (Oculomotor Nerve)

Cranial Nerve III (Oculomotor Nerve)

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Synonyms

CNIII; Cranial nerve III; Oculomotor nerve

Definition

The *oculomotor nerve* (cranial nerve III) begins in the midbrain, provides motor innervation to many of the extraocular muscles, and provides parasympathetic innervation to the eye. The third nerve begins in the third cranial nerve nucleus located at the level of the superior colliculus in the dorsal midbrain. The fascicular part of cranial nerve III then projects from the nucleus and travels ventrally, passing by the red nucleus, the corticospinal tracts, and other important brainstem structures. The fascicle exits the midbrain into the interpeduncular fossa and travels in the subarachnoid space medial to the cerebral peduncle.

In the subarachnoid space, the oculomotor nerve travels in close association to arteries of the circle of Willis. Specifically, CNIII travels in-between the posterior cerebral artery (PCA) and superior cerebellar artery (SCA). Aneurysms in the PCA or SCA can rarely compress CNII at this point and cause a pupil-involved third nerve palsy. However, because the posterior communicating artery (PCOM) runs parallel to CN III in this location, it is often an aneurysm of the internal carotid artery-PCOMM artery that produces the clinical finding of ipsilateral acute and often painful and pupil-involved CNIII palsy.

As the CNIII continues anteriorly, it enters the lateral wall of the cavernous sinus. Thus, pathology of the cavernous sinus may lead to third nerve palsies in isolation or in combination with other cranial nerves (e.g., IV, V1, V2, and VI) or Horner syndrome. Superior and inferior divisions of CNIII arise after CNIII exits the cavernous sinus. Both divisions of CN III enter the orbit through the superior orbital fissure.

In the orbit, the superior branch innervates the levator palpebrae and superior rectus muscle. The inferior division innervates the inferior rectus, inferior oblique, medical rectus, and ciliary ganglion. Parasympathetic fibers synapse in the ciliary ganglion and supply the pupillary constrictor and ciliary muscle for accommodation.

Cross-References

▶ Cavernous Sinus Syndrome
▶ Third Nerve Palsy

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Cranial Nerve IV

▶ Cranial Nerve IV (Trochlear Nerve), CNIV

Cranial Nerve IV (Trochlear Nerve), CNIV

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Synonyms

CN IV; Cranial nerve IV; Trochlear nerve

Definition

CN IV begins in the trochlear nerve nucleus located in the caudal mesencephalon, both ventral to the cerebral aqueduct and caudal to the oculomotor nucleus complex. CN IV fascicles derive from both nuclei, travel dorsally around the cerebral aqueduct, and decussate in the

anterior medullary velum just caudal to the inferior colliculi. Thus, the trochlear nerve emerges contralaterally between the inferior colliculi and superior cerebellar peduncles on the dorsal brainstem. The *trochlear nerve* is unique in that it is the only cranial nerve exiting from the dorsal brainstem as well as providing contralateral innervation to its target. Further, as will be detailed below, the fourth nerve has the longest intracranial pathway and thus is more vulnerable to trauma.

Once in the subarachnoid space, the CN IV travels ventrally around the cerebral peduncles to project toward the cavernous sinus and orbit. CN IV is positioned lateral to the oculomotor nerve (cranial nerve III) and passes between the posterior cerebral and superior cerebellar arteries. Aneurysms of these arteries may rarely lead to a fourth nerve palsy. Associated symptoms include vertical and torsional diplopia and an ipsilateral hypertropia and excyclotorsion on exam.

The fourth nerve then pierces the dura mater between the attached and free margin of the tentorium cerebelli and runs anteriorly along the lateral wall of the cavernous sinus. Therefore, pathologies of the cavernous sinus may also lead to fourth nerve palsy.

Upon passage through the superior orbital fissure, the *trochlear nerve* remains outside of the annulus of Zinn and lateral to the tendinous ring. The cranial nerve then travels medially to innervate the superior oblique muscle.

Cross-References

- ▶ Cavernous Sinus Syndrome
- ▶ Fourth Nerve Palsy

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Cranial Nerve V (Trigeminal Nerve)

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Synonyms

Trigeminal nerve

Definition

Cranial Nerve V provides sensation to the face as well as motor functions for the muscles of mastication. It is the largest of the cranial nerves and has three major branches, the ophthalmic (V_1), maxillary (V_2), and mandibular (V_3). The mandibular nerve is responsible for cutaneous and motor functions and develops from the embryonic pons basal plate, while the maxillary and ophthalmic are purely sensory and derive from the cranial neural crest. All three branches convene at the trigeminal ganglion within Meckel's cave, which is analogous to the dorsal root ganglia of the spinal cord in that it contains the cell bodies of sensory nerves. From this ganglion stems a single sensory root that enters the brainstem at the pons level. Dermatomes of the

branches are sharply delineated such that local anesthetic injection can anesthetize precise areas of the face and mouth.

Cross-References

- ▶ Gasserian Ganglion (Semilunar/Trigeminal Ganglion)
- ▶ Infraorbital nerve
- ▶ Trigeminal Ganglion (Gasserian/Semilunar Ganglion)
- ▶ V1 (Ophthalmic Nerve)
- ▶ V2 (Maxillary Nerve)
- ▶ V3 (Mandibular Nerve)

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Cranial Nerve VI (Abducens Nerve)

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Synonyms

Abducens nerve; CNVI; Sixth cranial nerve

Definition

The sixth cranial nerve (CNVI), or abducens nerve, is an efferent motor nerve that controls the ipsilateral lateral rectus muscle of the eye, which abducts the eye away from the midline (Binder et al. 2010). CN VI originates from the abducens nucleus, which is located on the lower portion of the dorsal pons in the brain stem. CN VI exits the pons at the pontomedullary junction, and it courses superiorly over the clivus, encased within a fibrous sheath (Dorello canal), and enters the dura just inferior to the posterior clinoid process. The sixth cranial nerve's long, oblique course over the clivus and its enclosure in the Dorello canal make it susceptible to injury due to compression or stretching of the nerve by increased intracranial pressure (ICP), trauma, aneurysm, or space-occupying lesions like tumor (Binder et al. 2010).

After piercing the dura, CN VI then courses over the medial petrous apex and into the cavernous sinus, where it then runs inferolateral and parallel to the internal carotid artery. CN VI then passes through the superior orbital fissure and into the orbit, where it innervates the ipsilateral lateral rectus muscle (Binder et al. 2010).

Sixth nerve palsy is a common neurological ocular motor palsy because of its long intracranial course and potential for stretching – especially over the clivus – which results in horizontal binocular diplopia (Spalton 2005). It may be congenital or acquired and unilateral or bilateral. Sixth nerve palsy may be caused by any lesions in the pons, subarachnoid space, cavernous sinus, or

orbit (e.g., inflammation, infection, trauma, neoplasm) or as a non-localizing finding of increased ICP (Friedman and Kaiser 2007).

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Cranial Nerve VII

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Synonyms

Facial nerve

Definition

Cranial nerve VII (CN VII) has regular and special sensory, regular and special motor, and autonomic (i.e., parasympathetic) functions. The CN VII is derived from the second pharyngeal branchial (hyoid) arch, with the motor division developing from the basal plate of the pons and the sensory from the embryonic cranial neural crest. The special sensory function of CN VII includes taste information from the anterior two-thirds of the tongue and oral cavity. There is also parasympathetic supply on CN VII to the submandibular and sublingual glands via the chorda tympani nerve for saliva flow. CN VII exits the brainstem between the pons and medulla to provide parasympathetic innervation to head and neck ganglia, while supplying the nasal mucosa and lacrimal glands. The main regular motor function of the CN VII is voluntary control of the muscles of facial expression as well as innervation of middle ear musculature (e.g., the nerve to the stapedius muscle). CN VII also serves as the efferent limb of the corneal reflex. The motor segment originates from the facial nerve nucleus in the pons with the parasympathetic and sensory portions rising from the nervus intermedius. After reaching the temporal bone, the CN VII divides into the internal auditory canal, labyrinthine segment, intratympanic segment, and descending or vertical segment. The nerve exits the stylomastoid foramen and enters the parotid to branch into its terminal segments. The facial nerve also forms the geniculate ganglion at the genu of the facial canal.

Etiology

Cranial nerve VII is responsible for idiopathic acute facial nerve paralysis such as Bell palsy and can result from viral infection or multiple cranial nerve ganglionitis. Paralysis can also result from other etiologies including Lyme disease or misplaced local anesthesia in inferior alveolar nerve block, inflammatory disease, and neoplasm.

Clinical Presentation

Since CN VII performs many functions, damage may lead to complex symptoms within a range of

severity, commonly leading to facial distortion. Most symptoms arise quickly and peak within 48 h. Presentation includes ipsilateral weakness of the face, saliva and tear production may be affected with increased drooling or drying of the eyes and loss of taste, and increased sensitivity to sound is possible (i.e., hyperacusis).

Diagnostics

Magnetic resonance imaging (MRI) or computed tomography (CT) may show an etiologic cause of CN VII palsy.

Therapy

The treatment of CN VII palsy should be directed at the underlying etiology. Corticosteroid and/or antiviral therapy has been recommended for some idiopathic or presumed postviral cases.

Prognosis

Although recovery is dependent upon treatment of the underlying etiology, most idiopathic cases recover normal function within 6 months.

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Cranial Sixth Nerve Palsy

► Sixth Nerve Palsies

Craniofacial Disjunction (Le Fort III)

► Le Fort Fractures

Craniopharyngiomas

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Definition

A craniopharyngioma is a rare, benign tumor of the sellar region that may present with disturbances in the hypothalamic-pituitary axis, the visual system, and the flow of craniospinal fluid (CSF).

Etiology

Craniopharyngiomas are generally considered to be embryonic vestigial epithelial remnants of the Rathke pouch located between the anterior and posterior lobes of the pituitary (Yanoff and Duker 2008).

Clinical Presentation

All of the clinical features are caused by the tumor encroaching upon the nearby structures of the brain. Compression of the optic chiasm causes a bitemporal often inferior quadrantanopia or an incomplete or complete bitemporal hemianopsia (Yanoff and Duker 2008). Whereas compression of the pituitary stalk or the gland itself can produce a wide variety of symptoms such as diabetes insipidus, eating disorders, and growth retardation or delayed puberty in children. In addition, patients often present with headaches due to the obstruction of CSF flow (Lumenta et al. 2010).

Diagnostics

The most important diagnostic tool is the magnetic resonance imaging (MRI) of the head and, in some instances, a computed tomography (CT) scan of the head as well. The MRI will typically show a cystic and solid tumor located in the sella often displacing and compressing the pituitary gland. The tumor itself usually contains one or multiple heterogeneous cysts often with calcification (Lumenta et al. 2010). Two distinct variants of the craniopharyngioma are seen upon histological examination. The adamantinomatous craniopharyngioma demonstrates cords of squamous epithelium with peripheral palisading and compact lamellar keratin formation known as "wet keratin." This subtype often contains cholesterol rich, thick brownish fluid that looks like "machine oil." Papillary craniopharyngiomas, the second subtype, contain both solid sheets and papillae lined by well-differentiated squamous epithelium (Kumar et al. 2010).

Differential Diagnosis

The two more common causes of the neuro-ophthalmologic manifestations found in patients with a craniopharyngioma are pituitary adenoma and meningioma, but other sellar lesions including aneurysm, inflammation, demyelination, infection, or metastases can mimic the clinical presentation (Lumenta et al. 2010).

Therapy

There are no medical treatments for craniopharyngiomas, so these tumors must be removed surgically. Residual or recurrent tumor may be treated with radiation therapy (Lumenta et al. 2010).

Prognosis

Craniopharyngiomas have a 10-year survival rate of over 90%, but there are often recurrences due to the locally invasive nature of the capsule. The combination of surgery and radiation limits the likelihood of recurrence (Lumenta et al. 2010; Prayson 2008).

Epidemiology

The occurrence of this tumor is bimodal with one peak in the first two decades of life and another peak in the sixth and seventh decades of life (Lumenta et al. 2010; Prayson 2008). These tumors represents 2–4% of intracranial neoplasms, 8–13% of pediatric intracranial neoplasms, 20% of suprasellar masses in adults, and 54% of suprasellar masses in children (Yanoff and Duker 2008).

Cross-References

► Parasellar Lesions

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CRAO

► Central Retinal Artery Occlusion, Ocular Ischemic Syndrome

CRVO

► Central Retinal Vein, Occlusion of

Cryoanalgesia

► Anesthesia, Cataract

Cryptophthalmos

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Definition

A congenital lid malformation where the lids are continuous with the underlying globe

Etiology

During development, the lids either completely or partially fail to separate from the underlying globe (Keefe et al. 2008; Gupta and Kim 2011). This leaves the conjunctiva and cutaneous epithelium as a continuous structure (Kersten et al. 2013).

Clinical Presentation

This is a congenital malformation. The complete form of cryptophthalmos has skin replacing normal eyelids and this skin connects to the underlying globe (Keefe et al. 2008). Usually this presents bilaterally, but there are reports of asymmetric unilateral cases (Gupta and Kim 2011; Sachdeva and Traboulsi 2013). There are no lashes or eyebrows and the individual may or may not have lacrimal glands and canaliculi (Gupta and Kim 2011; Dollfus and Verloes 2013). The globes may also be microphthalmic. On examination, there will be a small or absent anterior chamber due to severe dysgenesis with many of the anatomic structures replaced by connective tissue (Gupta and Kim 2011). There are multiple forms of cryptophthalmos:

- The complete form has lids replaced by layer of skin and do not have a conjunctival sac (Sachdeva and Traboulsi 2013). Cornea and conjunctiva are still present but dermoid transformation changes them into skin (Gupta and Kim 2011).
- The incomplete form has colobomatous lids with a conjunctival sac and an exposed opaque cornea (Dollfus and Verloes 2013; Sachdeva and Traboulsi 2013).
- A related disease is pseudocryptophthalmos. The normal cornea and conjunctiva are covered by skin of eyelids that failed to separate (Gupta and Kim 2011).

Diagnosis

Diagnosis is by clinical observation

Differential Diagnosis

Anophthalmos
Pseudocryptophthalmos
Microblepharon
Mesodermal corneal metaplasia

Prophylaxis

Unclear.

Therapy

Surgical repair is the only therapy and is only recommended in a few cases. Surgery for cryptophthalmos involves pedicle rotation flaps, skin grafts, and mucous membrane grafts to reconstruct the conjunctival surfaces (Kersten et al. 2013). Pseudocryptophthalmos can be surgically treated by simply creating a palpebral fissure (Gupta and Kim 2011).

Prognosis

Prognosis depends on the form of cryptophthalmos

- Complete: No chance of gaining vision due to the dermoid transformation of corneal and conjunctiva (Kersten et al. 2013)
- Incomplete: Vision may be improved and cosmesis improved, but this is unlikely (Kersten et al. 2013)
- Pseudocryptophthalmos: Excellent visual acuity but may have problems maintaining a functional eyelid (Gupta and Kim 2011)

Epidemiology

Very rare with only case reports available. Can be found as an isolated disease, but more than half have cryptophthalmos as part of Fraser syndrome (Keefe et al. 2008; Dollfus and Verloes 2013). The syndrome is inherited and is autosomal recessive (Gupta and Kim 2011).

Cross-References

▶ Cryptophthalmos-Syndactyly (Fraser) Syndrome

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Cryptophthalmos-Syndactyly (Fraser) Syndrome

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Synonyms

Fraser-François syndrome; Meyer-Schwickerath syndrome; Ullrich-Feichtiger syndrome

Definition

Fraser syndrome is a sex-linked recessive genetic condition that causes developmental defects. Ocular manifestations include cryptophthalmos, where the eyelids are fused together and failed to separate during development. Other developmental defects include fused fingers or toes (syndactyly), genital malformations, renal

maldevelopment, laryngeal stenosis, ear malformation, and mental retardation.

Cross-References

► Cryptophthalmos

Crystalline Corneal Dystrophy

► Crystalline Dystrophy

Crystalline Corneoretinal Dystrophy (Bietti)

► Corneal Dystrophies

Crystalline Dystrophy

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Synonyms

Crystalline corneal dystrophy

Definition

A group of hereditary, often progressive disorders characterized by symmetric bilateral crystalline deposits of varying depths of the cornea. Crystalline deposits are usually clear on indirect illumination, but may be white or gray with direct illumination.

The most common crystalline dystrophies broken down by corneal depth include:

1. Superficial cornea – Meesmann's dystrophy and gelatinous droplike dystrophy
2. Stromal cornea – lattice dystrophy, Schnyder's dystrophy, and Bietti's dystrophy (Holland et al. 2011)

Etiology

There is a high variability in terms of age of onset, genetic abnormality, and composition of crystalline substances observable in the cornea for crystalline dystrophies.

Clinical Presentation

1. Superficial Cornea
   - Meesmann's dystrophy – as early as infancy, photophobia, recurrent punctiform epithelial erosions, and lacrimation may present (Munier and Schorderet 2008). Bilateral, well-delineated intraepithelial cysts of 10–50 μm affect the entire cornea. These appear gray on direct illumination (Holland et al. 2011).
   - Gelatinous droplike dystrophy – irritation, redness, tearing, and decreased vision (Munier and Schorderet 2008) due to bilateral gelatinous amyloid deposits limited to the central cornea appear refractile on indirect illumination and take the shape of a mulberry (Holland et al. 2011).
2. Stroma
   - Lattice dystrophy – superficial amyloid dots in the central cornea radiate out (Munier and Schorderet 2008) to produce refractile lines with nodular dilations that are white in direct light and translucent or crystalline in indirect light (Holland et al. 2011). Recurrent epithelial erosions are common and a diffuse ground-glass haze develops (Munier and Schorderet 2008).

- Schnyder's dystrophy – progresses from a central cornea haze/subepithelial cholesterol crystal deposition to an arcus lipoides complicated by a midperipheral panstromal haze. Systemic findings include genu valgum and hypercholesterolemia (Jensvold and Tindall 2008).
- Bietti's dystrophy – nyctalopia, peripheral visual field loss, or central visual acuity loss. Glistening crystalline-like changes in the retina and crystals in the stromal cornea composed of cholesterol that can also be found in fibroblasts and circulating lymphocytes (Hinton et al. 2013). Associated retinal pigment epithelial atrophy and choroidal sclerosis can also present (Holland et al. 2011).

Diagnostics

Routine eye exam using slit lamp with special attention to depth and color of crystalline deposits, histopathologic examination of deposits, lab findings, and molecular genetic testing may all aid in the diagnosis of crystalline dystrophies (Munier and Schorderet 2008).

Differential Diagnosis

The differential diagnosis for a specific crystalline dystrophy includes the other diseases included under this general category.

Prophylaxis

None

Therapy

Patching, hypertonic agents, artificial tears, or therapeutic contact lenses for erosion. Surgically, anterior stromal micropuncture, superficial keratectomy, excimer laser ablation (phototherapeutic keratectomy), and lamellar or penetrating keratoplasty can be considered (Goldstein et al. 2014).

Prognosis

Dependent on specific dystrophy.

Epidemiology

Crystalline dystrophies, a subset of corneal dystrophies, are generally considered ubiquitous but rare conditions (<0.10% in the USA) with small pockets of high prevalence throughout the world (Musch et al. 2011).

Cross-References

- ▶ Bietti Crystalline Retinopathy
- ▶ Congenital Hereditary Stromal Dystrophy
- ▶ Corneoretinal Dystrophy, Bietti's Crystalline
- ▶ Juvenile Epithelial Dystrophy (Meesmann Dystrophy)
- ▶ Lattice Dystrophy
- ▶ Schnyder Crystalline Dystrophy Syndrome

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Crystalline Keratopathy, Infectious

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Synonyms

ICK

Definition

A spectrum of corneal infectious processes which share a branching, needlelike pattern of opacities within the corneal stroma (Keenan and McLeod 2013).

Etiology

Infectious crystalline keratopathy (ICK) is a less common form of bacterial corneal infection that is typically seen in corneal grafts. It has also been described in other conditions including chronic corticosteroid therapy, herpetic keratitis, and others. Current theory suggests that a colony of slow-growing organisms is implanted at the mid-stroma level in an immunocompromised cornea. Most cases have been attributed to the *Streptococcus viridians* group; however, many organisms, including some fungal species, have been associated with ICK (Reidy et al. 2011; Keenan and McLeod 2013).

Clinical Presentation

The most common presentation occurs several months status post penetrating keratoplasty. Symptoms are similar to those seen in other forms of infectious keratitis and include redness, photophobia, and conjunctival swelling. Discomfort can range from mild to severe. Examination of the patient shows conjunctival injection and chemosis. Slit lamp examination will reveal nonsuppurative stromal infiltrates. In the eyes with corneal grafts, the infiltrates will typically extend to the graft margin. The infiltrates can vary from fine and feathery to thick and arborizing. There may or may not be associated with epitheliopathy. The anterior chamber is usually quiet but hypopyon has been reported in the literature (Kinota et al. 1993; Reidy et al. 2011; Keenan and McLeod 2013).

Diagnosis

As with all corneal infectious processes, diagnosis is based on clinical and microbiological examination. Conjunctival swabs, as with many corneal infections, are low yield; therefore, deep corneal scrapings or corneal biopsy are the preferred method for species identification. Histopathological examination generally reveals pockets of gram-positive cocci between intact collagen lamellae without significant inflammatory cell infiltrate. Bacterial cultures and sensitivities should be obtained. The most commonly isolated organism is *Streptococcus viridians* (Kinota et al. 1993; Fillmore et al. 2007).

Differential Diagnosis

Central crystalline dystrophy of Schnyder, Bietti crystalline corneoretinal dystrophy, cystinosis, lymphoproliferative disorders, herpetic keratitis, and other forms of infectious and noninfectious keratitis (Ehlers and Shah 2008).

Prophylaxis

Due to the rare appearance of ICK, there are currently no guidelines for prophylaxis other than standard precautions used for penetrating keratoplasty.

Therapy

No specific guidelines have been identified specifically for ICK. Like all corneal infectious processes, therapy is initially focused on the most common causative organisms. Regarding ICK, the culprit is usually *Streptococcal viridians*. Fourth-generation fluoroquinolones, such as moxifloxacin, have relatively good activity against gram-positive organisms; however, some authors advocate fortified vancomycin as the primary treatment. Historically, aminoglycosides have also been used. The treating provider should consider susceptibility patterns found in the area and target therapy accordingly once a species has been identified. In some cases, systemic antibiotic therapy has been added (Kinota et al. 1993; Fillmore et al. 2007; Keenan and McLeod 2013).

Prognosis

Prognosis depends on the severity of the initial infection and the successful eradication of the bacteria. Stromal scars usually develop. Repeat penetrating keratoplasty is sometimes needed to optimize visual potential (Kinota et al. 1993).

Epidemiology

Exact prevalence is unknown. It is typically seen in patients who have undergone penetrating keratoplasty. It has also been reported with incisional keratotomy, contact lens use, chemical burns, chronic corticosteroid use, topical anesthetic abuse, and others (Keenan and McLeod 2013).

Cross-References

- ▶ Bacterial Keratitis
- ▶ Crystalline Dystrophy
- ▶ Keratitis

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Crystalline Lens

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Definition

The lens is a transparent biconvex structure inside the eye with the primary function of focusing light on the retina and changing the focus of the eye.

Anatomy

The lens consists of the lens capsule, the epithelium, cortex, and nucleus. It is held in its position between the iris and the vitreous cavity by the zonular fibers and has the ability to refract light because its refractive index (about 1.4 in the center and 1.36 in the periphery) is different from that of the aqueous humor and the vitreous (1.336) (Atchison and Smith 2002).

The lens capsule is a membrane enveloping the lens with a thickness between 5 and 25 μm consisting of collagen type IV. The anterior capsule is thickest in the midperiphery and thinnest at the anterior pole of the lens. The capsule on the posterior surface is likewise thinnest in the area of the posterior pole and thickens towards the periphery. Under the anterior capsule of the lens and at the lens equator the monolayered lens epithelium is found. The lens grows throughout life because the lens epithelium continues to generate new clear lens fibers with a hexagonal diameter which form several layers and thus constitute the lens cortex. The oldest fibers form the lens nucleus. At birth the equatorial diameter of the lens is about 6.4 mm, the central anteroposterior thickness, 3.5 mm, and the weight 90 mg. The adult lens measures about 9 mm in its equatorial diameter and 5 mm anteroposteriorly and weighs about 255 mg. In its distance-accommodated state the lens contributes 15–20 D to the total dioptric power of the human eye of about 60 D. With advancing age, the ratio of cortex to nucleus increases because the size of the nucleus remains stable. Also, the curvature of the lens increases with age. Therefore, older lenses should theoretically have a higher dioptric power than younger lenses. This effect is, however, balanced by an age-related shift in the refractive index, presumably due to accumulation of insoluble protein particles.

Development

The lens is of ectodermal origin. The development begins with thickened ectodermal cells overlying the optic vesicle and forming the lens placode which invaginates into the optic cup and finally becomes the lens vesicle with the cells turned inwards. With further differentiation these cells elongate into lens fibers and finally fill the lens vesicle entirely.

Physiology

The crystalline lens is the only transparent cellular structure in humans. Its transparency follows from several factors such as the lack of vascularization (the lens receives nutrients from the vitreous and aqueous humor), the lack of nuclei and organelles in the lens fibers, the regular and tight organization of the hexagonal fibers, and the production of transparent proteins.

The young human lens is able to change its shape due to the elasticity of the capsule and the lens material thereby changing the focus of the eye. This is achieved by the action of the ciliary muscle via slackening or tightening of the zonular fibers, a process called accommodation.

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Crystalline Stromal Dystrophy

▶ Schnyder Crystalline Dystrophy Syndrome

CSF

▶ Contrast Sensitivity Function, General

Cupid's Itch

► Syphilis: Overview

Curly Fiber Corneal Dystrophy

► Thiel-Behnke Dystrophy

Custom LASIK

► Wavefront-Guided Laser In Situ Keratomileusis

Cutaneous Horn

► Cutaneous Horn+B2658
► Papillomas, Eyelid

Cutaneous Horn+B2658

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Synonyms

Cutaneous horn; Hyperkeratosis

Definition

A lesion with extensive hyperkeratosis projecting in a protruding, sometimes conoid, manner.

Etiology

Thickening of the keratin layer from the base of a proliferative lesion, results in a cutaneous horn. The base lesion may be a benign, premalignant, or malignant lesion.

Clinical Presentation

Present as hyperkeratotic papules that protrude from the skin, usually several millimeters in height. They are more common in sun exposed areas.

Diagnostics

Biopsy of the base of the lesion is required to determine if malignancy is present. The majority of lesions are benign, but 20% of lesions may be premalignant or malignant (Albert and Jakobiec 2008).

Differential Diagnosis

Actinic keratosis
Squamous cell carcinoma
Seborrheic keratosis
Verruca vulgaris
Basal cell carcinoma

Prophylaxis

Sun exposure and UV protection may be recommended, based on the type of lesion at the base of the cutaneous horn.

Therapy

Biopsy of the base of the lesion is required to determine if malignancy is present. Benign lesions do not require further therapy; however, malignant lesions will require surgical excision with appropriate margins.

Prognosis

Prognosis is dependent on the lesion present at the base. Follow-up examinations are necessary for new or recurrent lesions.

Epidemiology

Cutaneous horns tend to be more common later in age in those with a history of sun exposure and of fairer complexions.

Cross-References

- Actinic Keratosis
- Basal Cell Carcinoma of Eyelid
- Seborrheic Keratosis
- Squamous Cell Carcinoma of Eyelid
- Verruca Vulgaris

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Cutler-Beard Procedure

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Synonyms

Bridge flap technique; Lid sharing procedure

Definition

A lower eyelid sharing technique in which a full-thickness flap of skin muscle and conjunctiva are developed from beneath the lower eyelid margin and advanced into an extensive upper eyelid defect for reconstruction.

Indication

The Cutler-Beard procedure is used to reconstruct extensive (usually 50% or more) full-thickness upper eyelid defects involving the eyelid margin.

Contraindications

An intact healthy lower eyelid is required for the reconstruction. The flap will remain closed for usually a minimum of 6 weeks completely obstructing vision out of the ipsilateral eye; therefore, a seeing eye on the contralateral side is required for vision. The Hughes flap should be avoided in monocular patients or in children at risk of amblyopia development.

Techniques and Principles

Extensive upper eyelid defects require reconstruction for viability and protection of the eye. On occasion, these extensive upper eyelid defects mandate utilization of an otherwise normal lower eyelid for reconstruction in the form of a Cutler-Beard procedure.

Surgery begins with an assessment of the defect size. The proximal and distal cut ends of the eyelid are grasped with forceps, and any slack is gently removed so the defect size can be accurately measured. After marking the lower eyelid for an appropriately sized flap to reconstruct the upper eyelid, a full-thickness incision is made 5 mm below the lower eyelid margin. The incision is facilitated by placing an eyelid plate or malleable retractor into the inferior fornix as a backstop for globe protection. An incision in this location is designed to preserve the marginal arcade blood supply to prevent ischemia of the lower eyelid margin bridge. Back cuts are made perpendicular to the infraciliary incision extending into the inferior fornix to allow superior mobilization of this flap which consists of lower eyelid skin, orbicularis oculi muscle, and conjunctiva/lower eyelid retractors. The flap is then separated into layers: conjunctiva, orbicularis oculi muscle, and skin with scissors. The conjunctiva of the

inferiorly based flap is sutured to residual upper eyelid conjunctiva with absorbing sutures. The inferiorly based orbicularis oculi muscle is then sutured to residual levator muscle if present, and inferiorly based skin is sutured to residual upper eyelid skin to complete three-layer closure. A modified procedure exists in which a tarsal substitute, such as ear cartilage, is sandwiched between the skin and muscle as a tarsal substitute.

Separation of the flap is carried out usually 6–8 weeks later. The tissue bridge is divided with a scalpel or scissors. The opening should be beveled such that the conjunctival side is approximately 2 mm longer than the skin side. This encourages healing with mucosal tissue at the new eyelid margin as opposed to keratinized tissue which can abrade the cornea.

The lower eyelid is then reformed by freshening the inferior border of the lower eyelid margin bridge and suturing this border to the divided full-thickness tissue bridge. Postoperative edema of the eyelid can persist for 4–6 weeks after which the newly reconstructed upper eyelid usually begins to assume a more normal appearance and function.

Outcome

This is a two-stage procedure, which can often achieve a functional upper eyelid capable of providing adequate protection of the globe when extensive tissue loss is present. The reconstructed eyelid however is often thickened with limited mobility and devoid of lashes.

Complications

Upper eyelid entropion can occur with subsequent corneal irritation and decompensation. Some authorities feel that modification of the procedure with placement of a tarsal substitute may decrease the probability of this outcome. Lower eyelid scarring and malposition, usually ectropion, may result. Loss of the lower eyelid margin bridge secondary to ischemia will result in significant lower eyelid deformity.

Cross-References

▶ Eyelid Reconstruction

References

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Cyanoacrylate Adhesive

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Synonyms

Dermabond; Histoacryl; Histoacryl Blue; Indermil; Nexacryl

Definition

Cyanoacrylates are esters of cyanoacrylic acid. These are monomers that harden by polymerization through contact with fluids such as water or blood. Hydroxylation occurs and results in varying tensile strengths depending on the type of cyanoacrylate derivative. The application of this rapidly polymerizing glue can restore structural integrity to any surface with which it comes in contact.

Indication

The most extensively documented uses of cyanoacrylate tissue adhesive are in treatment of impending or frank corneal perforations, as well

as descemetoceles. In these cases the glue acts as a barrier between the cornea and inflammatory cells and other collagenase-secreting cells in the tear film. The best outcomes occur in perforations less than 1–2 mm in diameter, although successful treatment of perforations up to 3 mm has been reported with the use of cyanoacrylate glue. Frequently, cyanoacrylate tissue adhesives are used as a temporizing measure until a definitive procedure such as a penetrating keratoplasty can be performed. Given evidence that in both infectious and traumatic perforations corneal transplantation has better outcomes if it can be delayed until the eye is less inflamed, tissue adhesives have come to play a vital role.

Furthermore, glue can be used for wound leaks, filtering bleb leaks, punctual occlusion, skin closure in oculoplastics, securing of hard/rigid contact lenses in severe ocular surface disease, treatment of amblyopia, and temporary tarsorrhaphy in corneal exposure.

Contraindication

There are no reported contraindications to the use of cyanoacrylate glue in the literature. Perforations larger than 2–3 mm or with significant surrounding necrotic tissue may not be amenable to adhesive repair. Of note is that the Food and Drug Administration (FDA) has not yet approved the use of tissue adhesives in the human eye, so such use is considered "off label."

Techniques and Principles

Principle: In addition to restoring structural integrity and providing a mechanical barrier to the outside world, application of cyanoacrylate glue to the ulcer bed interrupts progressive corneal stromal melting. The proposed mechanism is via the inhibition of polymorphonuclear leukocytes (PMNs). PMNs have been shown to produce collagenolytic enzymes that are key players in corneal melt. Furthermore, PMNs themselves have collagenolytic and proteolytic activity. For best results, it is best to apply cyanoacrylate early on, before overwhelming PMN infiltration has occurred.

Furthermore, cyanoacrylate glue has been found to have significant antibacterial effect. Specifically, glue has significant bacteriostatic activity against Gram-positive organisms (*Staphylococcus aureus*, *Streptococcus pneumonia*, and group A streptococci) but virtually no effect on Gram-negative microbes. The proposed theory underlying this difference has to do with the lipopolysaccharide capsule surrounding the cell wall in Gram-negative organisms which serves as barrier to the glue.

Techniques: Many techniques for application have been described, many of which are based on the same principles and differ only with regard to instruments and applicators used to apply the adhesive. All techniques have one common goal in mind: to use the minimum amount of glue to plug the perforation. If possible, the application of glue should be performed in a minor surgery room with an operating microscope and with the patient supine; however this can also be done in the office at a slit lamp if necessary. On a side table, the tissue adhesive is drawn up in a TB syringe with a 30-gauge needle or dental micropipette. Several drops of topical anesthetic are placed in both eyes and an eyelid speculum is gently inserted into affected eye. The 1–2-mm area of epithelium surrounding the ulcer is then debrided with cellulose spear because the glue does not adhere to epithelium. The perforation site is then carefully dried with a cellulose sponge in one hand, while the other hand uses the 30-gauge needle or micropipette to place one drop of tissue adhesive on the surface. The glue should solidify completely within a few minutes. Too much glue may cause the patient significant discomfort since its polymerized surface is rough, even with the bandage contact lens. Additional applications may be necessary. Alternatively, a flat sheet or drape can be used to apply the glue to the ocular surface and can be left in place resulting in a smoother surface. The area should then be inspected for aqueous leak before the application of bandage contact lens (BCL), which is preferably a low-water-content, high-Dk extended-wear silicone-hydrogel soft contact lens with a flat base curve.

Postoperative management includes placing the patient on topical and/or systemic aqueous suppressants as well as prophylactic broad spectrum topical antibiotics three to four times per day. For surface lubrication and to protect BCL, preservative-free artificial tears should be used at least four times a day. Lastly, a protective shield should be placed on the eye. Ideally, the glue should remain in place for weeks to months to allow for stromal healing and vascularization to occur. It typically loosens enough with time to provide for easy removal or spontaneously dislodges. The BCL should be replaced every 2–3 months.

Outcome

The literature focuses mostly on the use of cyanoacrylate glue in the management of corneal perforations. Outcomes in this subset of people have been largely good, and there is a clear benefit to the management of corneal perforations and descemetoceles with this technique. Studies have shown improved visual outcomes with reduced enucleation rates. While corneal patching with cyanoacrylate glue has traditionally been thought of as a temporizing procedure until more definitive surgical treatment can be performed, a significant subset of patients needed no further intervention.

Complications

The main concern with corneal application of cyanoacrylate glue is tissue histotoxicity, which occurs through the accumulation of breakdown products and increases with tissue vascularity. For this reason, there is more concern for toxicity with glue application to conjunctiva, sclera, or skin than to the corneal epithelium and stroma. However, most problems occur with inadvertent instillation of glue into structures such as the anterior chamber; this can result in polymerization over the corneal endothelium and iridocorneal and iridolenticular adhesions.

There is also increased risk for superimposed microbial keratitis the longer the glue remains in place. This is likely not because of the glue itself, but rather a consequence of the prolonged use of a therapeutic BCL. The risk has been shown to be increased especially once glue has been present for more than 6 weeks. Additional reported complications include glaucoma, giant papillary conjunctivitis, and retinal toxicity.

Cross-References

- ▶ Corneal Ulcers
- ▶ Descemetocele
- ▶ Keratolysis (Corneal Melting), Marginal, Systemic Immune-Mediated Disease

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Cyclocephaly

▶ Cyclopia

Cyclopia

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Synonyms

Cyclocephaly

Definition

Cyclopia is the most severe ocular abnormality and the most extreme form of holoprosencephaly, a cephalic developmental disorder in which the forebrain of the embryo fails to develop into two hemispheres, allowing structures that are normally paired on the left and right to merge. In cyclopia, two separate orbital cavities fail to develop during embryogenesis. This congenital condition is very rare.

Etiology

A number of teratogenic risk factors have been noted in association with the development of holoprosencephaly. Among these are gestational diabetes, exposure to transplacental infections, hypercholesterolemia, consanguinity, and female sex. Other possible teratogenic factors include exposure to ionic radiation, contraceptives, rubella vaccine, nicotine, anticonvulsants, antibiotics, amidopyrine, and alcohol.

Sporadic and inherited disruptions of the sonic hedgehog pathway have been reported to cause holoprosencephaly with cyclopia. The sporadic form occurs more frequently than the familial. The sonic hedgehog pathway gives cells information needed for proper embryonic development. There are at least four genetic regions that are implicated in the pathogenesis of holoprosencephaly. Sonic hedgehog is the only one of three homologous vertebrate genes to be expressed early in the midline of the developing central nervous system. It is expressed in the ventral forebrain and eye.

Clinical Presentation

The clinical presentation of holoprosencephaly can vary from true cyclopia, which is incompatible with life, to midfacial clefting. It is divided into three subtypes: alobar, semilobar, and lobar holoprosencephaly. The degree of CNS involvement dictates the clinical presentation of holoprosencephaly. In alobar holoprosencephaly, the brain consists of a single spherical forebrain structure with a single ventricle. Infants with the severe alobar form die after birth. The brain is missing the midsagittal fissure, corpus callosum, and olfactory bulbs and tracts are almost always absent. This form is most commonly associated with true cyclopia.

In true cyclopia, the fetus or infant presents with one central eye. The anterior brain and the midline structures do not develop normally. The result is a central cavity or pseudo-orbit with a proboscis but without a nasal cavity. In synophthalmia, the two globes are partially fused in the center. The head can be small for the age or of normal size with a proboscis over a central opening for the single or fused eye.

Differential Diagnosis

Synophthalmia

Prophylaxis

Avoidance of ingested or environmental teratogenic factors.

Prognosis

Cyclopia is not compatible with life due to the accompanying CNS abnormalities.

Epidemiology

Cyclopia can occur in all races and has been reported more frequently in females than in males. One case series reported an incidence of 1/40,000 births while the frequency of cyclopic fetuses was estimated between 1/250 and 1/500. Holoprosencephaly has a prevalence of 1:16000 live births and 1:250 during embryogenesis.

The estimated median maternal age is 35 years.

Cross-References

► Chromatic Aberration: Definition

Further Reading

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Cylindroma

► Cylindroma of Eyelid

Cylindroma of Eyelid

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Synonyms

Adenoid cystic carcinoma; Cylindroma

Definition

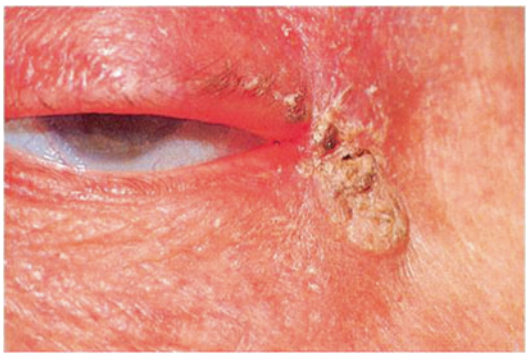
Benign sweat gland tumors involving the head, neck, and scalp. They are rare on the eyelids and brow.

Basic Characteristics

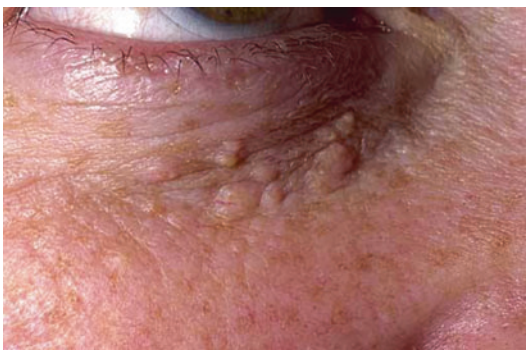
The tumor was previously thought to be of apocrine gland origin; however, more recent immunohistologic studies suggest the tumor exhibits apocrine, eccrine, secretory, and ductal features. It may be seen in combination with spiradenomas and trichoepitheliomas. There have been rare reports of malignant transformation.

Cylindromas present sporadically as slowly growing, singular, dome-shaped, pink rubbery nodules, varying in size from a few millimeters to several centimeters, usually on the scalp and face. Cylindromas are asymptomatic, presenting in middle age or later (Figs. 1 and 2).

In familial cylindromatosis or Brooke-Spiegler syndrome, an autosomal dominantly inherited disease, multiple cylindromas and other dermal appendage tumors may be present. Multiple larger lesions develop shortly after puberty. They may occur profusely on the scalp, in which they may be referred to as turban tumors. The proposed gene responsible in this condition is the CYLD gene on chromosome 16q12-q13. It is thought



Cylindroma of Eyelid, Fig. 1 Cylindroma of eyelid and canthus



Cylindroma of Eyelid, Fig. 2 Cylindroma of eyelid and canthus

to be a tumor suppressor; however, the exact function of this gene is not fully understood (Kim et al. 2007; Albert and Jakobiec 2008).

Cross-References

- ▶ Eccrine Spiradenoma
- ▶ Hidrocystoma, Apocrine
- ▶ Porosyringoma

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Cyst of Moll

- ▶ Hidrocystoma, Apocrine

Cystic Hidradenoma

- ▶ Hidradenoma, Clear Cell (Eccrine Acrospiroma)

Cystic Retinal Tufts

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Solitary or multiple, small, discreet, round or oval, elevated, white vitreoretinal lesion at the peripheral retina, composed primarily of glial tissue and represent visible sites of vitreoretinal adhesions. Vitreous condensations are attached to its surface, and its base may have pigmentary changes. It is congenital and is a potential cause of retinal tears and detachments following partial or complete posterior vitreous detachment.

Cysticercosis, Orbital Involvement and

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Definition

Parasitic infection by *Cysticercus cellulosae* (larval form of *Taenia solium*).

Etiology

Human infection caused by ingestion of contaminated water or uncooked vegetables infested with eggs of the worm and autoinfection.

Clinical Presentation

May present in many periocular and ocular locations including subconjunctival, intraocular, extraocular, eyelid, and intraorbital muscles or elsewhere causing related symptoms such as motility restriction, mass lesion, orbital cellulitis, and dacryoadenitis.

Diagnostics

Clinical examination, orbital imaging, B-mode ultrasonography.

Differential Diagnosis

Orbital cellulitis, orbital inflammatory diseases, orbital and ocular infectious disease.

Prophylaxis

Avoidance of eating and drinking uncooked vegetables or food and water in endemic areas.

Therapy

Systemic antiparasitic agents such as albendazole. Prednisone as an adjunctive measure has been used. Primary surgical excision is also possible.

Prognosis

Local sequelae such as proptosis, ptosis, motility defects, diplopia, or strabismus may be seen.

Epidemiology

Endemic in regions with poor sanitation. Ocular and orbital infection seen in 13–46% of systemic disease. Most common form of systemic disease is neurocysticercosis.

Cross-References

- ▶ Orbital Cellulitis
- ▶ Orbit, Inflammation of

Further Reading

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Cystinosis, Ocular Findings in, Retinal Degeneration

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Definition

Cystinosis is a rare autosomal recessive metabolic disorder characterized by the intracellular accumulation of cystine, the disulfide of the amino acid cysteine (Tsilou et al. 2007).

A pigmentary retinopathy has also been seen in cystinosis patients. This finding precedes the appearance of the crystals in the cornea and has been seen as early as 5 weeks of age or even in fetal life. However, pigmentary retinopathy does not appear to be a constant finding in cystinosis (Wong et al. 1967; Tsilou et al. 2007).

Clinical Presentation

The most commonly described ophthalmoscopic findings are pigmentary changes consisting of patches of depigmentation with pigmentary mottling at the periphery of the fundus and the macula. In the early stages the pigmentary abnormality is confined to the periphery, and the changes are more marked in the temporal than the nasal segments and appear bilateral and symmetric. In older patients the changes are seen more posteriorly. However, the macular abnormalities have been described as early as 6 years of age (Wong et al. 1967).

Usually there is no abnormality in visual function that accompanies the early findings (Wong et al. 1967). Because of successful renal transplantation and cystine depleting therapy, cystinosis patients are living longer and manifest the long-term complications of the disease, including the retinal degeneration. At the advanced stage, decreased visual acuity can result from both anterior and posterior segment complications (Dufier et al. 1987a). Decreased color, peripheral and night vision are often encountered by older cystinosis patients (Tsilou et al. 2007).

Fluorescein angiography reveals window defects corresponding to the patches of depigmentation, and indocyanine green videoangiography reveals a submacular choroidal neovascular membrane with feeder vessel. Intraretinal crystals are also detected (Tsilou et al. 2007).

Humphrey visual fields and electroretinography can confirm the presence of the retinopathy.

The histopathologic findings are poor as due to their water solubility, most cystine crystals are lost in aqueous fixatives. When processed in absolute alcohol, however, the crystals are identified within intracellular, single membrane-bound lysosomes. Rare crystals have been reported in the retina.

Focal degeneration has been frequently noted in the retinal pigment epithelium, and pigment migration into the inner retina has been seen on occasion. Focal destruction of the outer segments of the photoreceptors has also been reported (Francois et al. 1972; Dufier et al. 1987b). Ultrastructural examination showed numerous electron transparent polygonal spaces bounded by a single membrane in or adjacent to the lysosomes of the retinal pigment epithelial cells and in some choroidal resident cells (Tsilou et al. 2007).

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Cystotomy

► Capsulotomy

Cytomegaloviruses, Retinitis

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Synonyms

CMV retinitis

Definition

A slowly progressive, necrotizing retinitis that may appear as granular or hemorrhagic lesions associated with cytomegalovirus virus infection.

Etiology

Cytomegalovirus (CMV) is a double-strand DNA virus and the largest member of the herpesvirus family (230 kb). The prevalence of CMV infection among individuals aged >6 years old was found to be around 60%, and it seems that most people are exposed to CMV throughout their life. Like many other herpesviruses, CMV remains latent in the host and may reactivate if host immunity is compromised, especially in cases with a compromised cell-mediated immune system (AIDS, transplant recipients or patients with malignancy, or autoimmune disease with iatrogenic immunosuppression). Although majority of CMV retinitis cases affect immunosuppressed patients, there are few reports on CMV retinitis among immunocompetent individuals previously exposed to CMV with comorbid diabetes mellitus, hypertension, or hypercoagulable states. Congenital CMV is the most common perinatal systemic viral infection and is found in nearly 1% of all live births in the United States. Most of infected neonates will be asymptomatic. The incidence of CMV retinitis has been reported as high as 25% of infants with severely symptomatic congenital CMV, but some cases were also reported among asymptomatic infants (Whitcup 2010; Radwan et al. 2013).

Clinical Presentation

Patients may appear asymptomatic as lesions' location infrequently begins in the macular area, therefore usually vision can be nearly normal. Symptomatic patients may complain of blurred vision:

- There are two types of clinical appearances:
  - Indolent type: mild granular appearance with a few punctate hemorrhages,

sometimes with atrophic retina, and no vasculitis. It starts in the periphery and progresses slowly.
  - Fulminating type: yellow-white lesions that may become confluent, associated with retinal hemorrhages and perivenous vasculitis ("cottage cheese with catsup" or "pizza pie"). As compared to the indolent type, it progresses much faster (Figs. 1 and 2).
- Both types may be associated with a mild vitritis and sometimes fine anterior chamber reaction with pigmentary cells and keratic precipitates.
- The disease progresses slowly at approximately 250 μm/week. The disease may progress in two distinct ways: first and most common, new lesions spread from old lesions' borders. The active border generally advances posteriorly. Therefore new lesions may appear along with old atrophic lesions and mottled pigmentation of the RPE. Second is via hematogenous spread, in which new lesions will be found away from an old lesion.
- Lesions may be distributed along major retinal vessels.
- Among HIV patients CMV retinitis may present with frosted branch angiitis (Whitcup 2010).

Complications

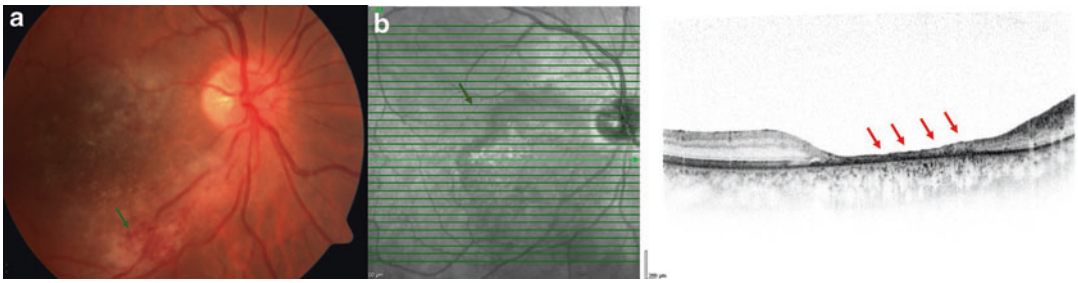
- Macular complications include retinal necrosis, cystoid edema, and epiretinal membrane; all can cause a severe permanent visual loss.
- Optic disk involvement may cause severe vision loss even with a mild retinitis.
- Retinal detachment may develop in approximately 20% of the patients. It can appear even after months to years post-initial diagnosis. Risk for developing retinal detachment is greater in the eyes with significant amount of peripheral retinal involvement. Mechanism proposed for this complication is probably a vitreous traction of the thinned, atrophic retina and the presence of retinal breaks (Fig. 3) (Whitcup 2010).

Diagnostics

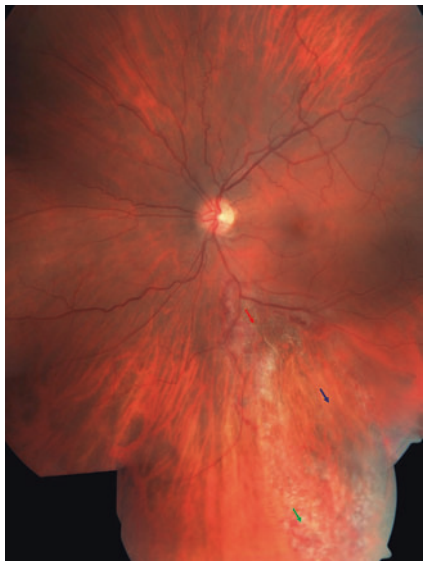
- Diagnosis is usually based upon clinical appearance and history.
- The disease can be confirmed by the demonstration of CMV DNA in aqueous, vitreous, and serum samples by polymerase chain reaction (PCR).
- Serial serum PCR results may aid in disease monitoring (Whitcup 2010).

Ocular Imaging

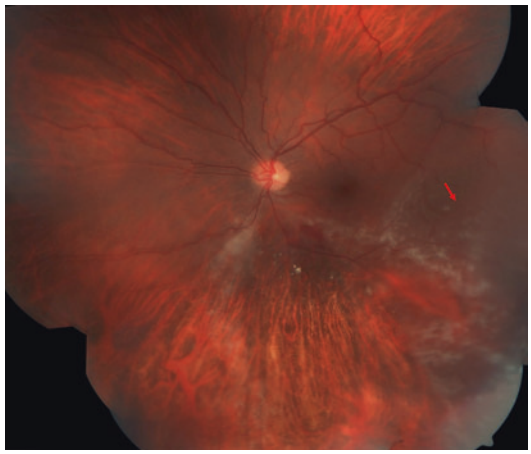
- Serial fundus photographs help the clinician assess retinitis progression and treatment course.
- Autofluorescence imaging is valuable in detecting and localizing active CMV retinitis. A hyperautofluorescent signal is correlated with the border of advancing CMV retinitis. Stippled areas of alternating hyperautofluorescence and



Cytomegaloviruses, Retinitis, Fig. 1 (**a**) Fundus color picture (right eye): acute phase of CMV retinitis, fulminating type, involving the posterior pole showing confluent white lesions with hemorrhages (*green arrow*); (**b**) spectral domain OCT demonstrating atrophic neurosensory retina 3 months later (*red arrows*)



Cytomegaloviruses, Retinitis, Fig. 2 Fundus color picture of the left eye with fulminant-type CMV retinitis demonstrating peripheral confluenting white lesions with hemorrhages (*green arrow*), atrophic area posterior to the lesions (*blue arrow*), and recent newer lesions (*red arrow*)



Cytomegaloviruses, Retinitis, Fig. 3 Fundus color picture of the left eye with fulminant CMV retinitis complicated by temporal retinal detachment (*red arrow*)

hypoautofluorescence are observed in regions of retinal pigment epithelium atrophy from prior CMV retinitis.

– Fluorescein angiogram used to assess areas of ischemia. Findings may include blocking defects from hemorrhages and leaking or non-perfusion of vessels in involved areas of retina.
– Spectral Domain Optical Coherence Tomography (SD-OCT) imaging demonstrates loss of architecture and significant atrophy. In some eyes vitreoretinal gliotic bands on top of the retina and connected to the cortical vitreous may be found at the border of normal and affected retinas. These bands may be a source of vitreoretinal traction leading to potential complications such as retinal breaks or retinal detachment (Fig. 1b).

Differential Diagnosis

Acute retinal necrosis syndrome (ARN) – usually appears in immunocompetent patients, in the periphery with an occlusive arteritis, significant vitritis, and a rapid disease progress. The disease may be caused by VZV, HSV1, and HSV2 and rarely by CMV and Epstein-Barr virus.

Progressive outer retinal necrosis (PORN) – herpetic retinitis that occurs in patients with AIDS and CD4 T-cells counts $\leq$ 200 cells/µl. It is characterized by extensive, rapidly progressing full-thickness necrosis of the retina involving initially the posterior pole, with little or no inflammatory component, and spares the retinal vasculature.

Toxoplasmosis – usually has a typical scar appearance adjacent to an active lesion. However, among immunocompromised patients toxoplasmosis may mimic a CMV retinitis.

Syphilis and *Behcet's disease* may also resemble CMV retinitis (Whitcup 2010).

Therapy

The goal of treatment is to preserve vision and prevent further disease progression. As CMV retinitis is a systemic infection that may affect also the fellow eye and other organs, patients should receive systemic therapy, with or without concurrent local treatment. Management consists of drugs with selective inhibition of viral DNA polymerase (virostatic) and includes induction and

maintenance phases. During the induction phase, the drug is given for 2–3 weeks or until clinical response is seen, and thereafter the drug dosage is reduced and is given for a long period of time, usually months. The CDC (Center of Disease Control) recommends continuing treatment to immunocompromised patients until CD4 T-cell values rise above 100 cells/μL for at least 3–6 months. During the entire treatment period, patients should be monitored closely for active cytomegalovirus retinitis lesions, and treatment should not be stopped until all lesions have become inactive (Whitcup 2010).

Intravenous Therapy

- Ganciclovir (Roche Pharmaceuticals, NJ) is the first FDA-approved drug (1989) for CMV retinitis. It is given twice daily at a dose of 5 mg/kg for 2–3 weeks (induction phase) and then the same dose daily as maintenance for weeks to months. Adverse effects include bone marrow suppression including neutropenia, anemia, and thrombocytopenia; therefore, complete blood count test should be done frequently.
- *Foscarnet* (Foscavir, AstraZeneca, Wilmington, DE), the second drug approved by the FDA (1991). It is also administrated intravenously with 2–3-week induction dosage (60 mg/kg three times a day or 90 mg/kg twice daily). Foscarnet was found to be less toxic to the bone marrow than ganciclovir; however, it is nephrotoxic and leads to electrolyte abnormalities. Therefore kidney function test should be done regularly and patient should be told to require adequate hydration.

  At the SOCA trial (Studies of Ocular Complications of AIDS) published at 1992, newly diagnosed CMV retinitis patients were randomized to either ganciclovir or foscarnet. Both drugs were found to be equally effective.
- Cidofovir (Vistide, Gilead, Foster City, CA), the third drug approved by FDA (1996). Induction consists of 5 mg/kg once weekly for 2 weeks and then the same dose every other week. It may cause dose-dependent nephrotoxicity and therefore intravenous hydration should be used with each treatment. It has been proved as replacement therapy for failure of ganciclovir and/or foscarnet (Whitcup 2010).

Oral Treatments

- Valganciclovir (Valcyte, Roche). An L-valyl ester prodrug of ganciclovir, approved by the FDA (2001). Unlike oral ganciclovir it has good bioavailability properties, ten times higher than oral ganciclovir, and can be used to both induction and maintenance phases. Nowadays it is considered to be the standard of care for CMV disease. Dosing should begin with a 900 mg twice a day for 3 weeks and then reducing to 900 mg per day for the maintenance phase. Main adverse effect includes pancytopenia, in addition to nausea, vomiting, seizures, confusion, and peripheral neuropathy. It is category C drug with reproductive toxicity and therefore should not be given to pregnant women. Complete blood count test should be done frequently (Whitcup 2010; Heiden et al. 2014).

Intraocular Injections

Intravitreal injections may be given as an adjunctive to systemic treatment in cases of sight-threatening retinitis (zone 1 disease) or as replacement therapy when systemic treatment is contraindicated or intolerated:

- Ganciclovir – Dosage is 2 mg/0.1 ml per injection twice a week in the induction phase and then once a week for maintenance. The low cost of the drug enables wide use in developing countries as replacement to systemic treatment. However, using only intravitreous treatment may endanger the fellow eye and other organs.
- Foscarnet – Dosage is 2.4 mg/0.1 ml per injection twice a week in the induction phase and then once a week for maintenance (Whitcup 2010).

Antiviral Resistance

Mutations in the CMV UL97 gene, a viral phosphotransferase necessary for ganciclovir activation, confer low-level resistance to ganciclovir,

while mutations in both the CMV UL97 and CMV UL54 genes lead to high-level ganciclovir resistance. In such cases treatment with either foscarnet or cidofovir is recommended (Whitcup 2010).

CMV Retinitis Among Human Immunodeficiency Virus (HIV) Patients

Before the availability of highly active antiretroviral therapy (HAART), CMV retinitis affected 25% of patients infected with HIV, having CD4 T-cell values below 100 cells/μL. As HAART treatment suppresses HIV replication, HIV load declines and CD4 T-cell values rise with an immune recovery. As a result, the incidence rates of CMV retinitis have declined. The LSOCA (Longitudinal Studies of the Ocular Complications of AIDS) study reported that the 4-year cumulative incidence of CMV retinitis among HIV patients treated with HAART, with CD4 T-cell values below 100, was 7%, a 72% reduction as compared to the pre-HAART area. In fact, only 12% of patients who had severe immunodeficiency (i.e., a CD4 T-cell count below 50 cells/μL) developed CMV retinitis during the first 4 years following the diagnosis of AIDS, a 52% reduction as compared to the pre-HAART area. However, HIV patients remain at risk for developing CMV retinitis either because of delayed diagnosis of HIV infection or because they are noncompliant with, intolerant of, or unresponsive to HAART treatment, as was recently reported by the WHO. Nevertheless, CMV retinitis remains the most common ocular opportunistic infection in patients with AIDS; hence, frequent screening is mandatory to detect the disease before it becomes sight threatening (Sugar et al. 2012).

Immune Recovery

Recovering of the immune system can control CMV retinitis without the need for ongoing prophylactic therapy. However, HAART has also been associated with the development of immune recovery uveitis (IRU) in nearly 20% of patients with CMV retinitis. IRU may induce vision loss, mainly from vitritis, macular edema, epiretinal membrane, and cataract. Corticosteroids are the mainstay of therapy for IRU patients (Whitcup 2010).

Cross-References

▶ Acute Retinal Necrosis (Necrotizing Herpetic Retinitis)

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D

Dacryoadenitis

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Definition

Acute or chronic inflammation of the lacrimal gland.

Etiology

Dacryoadenitis is classified as acute or chronic based on speed of onset and duration of symptoms. Acute dacryoadenitis is typically viral, bacterial, or inflammatory (a subset of idiopathic orbital inflammation, IOI) in origin. Chronic dacryocystitis is more likely to be associated with systemic conditions such as sarcoid, Wegener's granulomatosis, Sjögren's syndrome, or Graves' disease (Karesh et al. 2006). Rare infectious causes of chronic dacryocystitis include tuberculosis, leprosy, syphilis, Lyme disease, and trachoma.

Clinical Presentation

Symptoms often develop rapidly over hours to days, although chronic and atypical cases may have an insidious onset. The lacrimal gland is enlarged and easily palpated in the superotemporal orbit. This classically produces an "S-shaped" deformity of the upper eyelid, with swelling and mechanical ptosis more prominent laterally. With significant gland enlargement, the globe may be displaced inferomedially. The upper eyelid is typically painful and tender with prominent inflammatory signs. Chemosis, conjunctival injection, and discharge also may be present. Dacryocystitis is usually unilateral. Bilateral enlargement can be seen in up to half of lacrimal gland-involving pediatric IOI, but the likelihood of systemic disease is increased. Children may have constitutional signs and symptoms, including fever, malaise, loss of appetite, and nausea.

Diagnosis

Most cases are diagnosed clinically and empiric therapy is instituted. If present, discharge can be cultured to guide antibiotic coverage. Biopsy is reserved for atypical presentations and nonresponders (Guo et al. 2012). If bloodwork is done, increased ESR and eosinophilia are frequently present. Imaging is often helpful. On CT scan, dacryoadenitis appears as ill-defined enlargement of the lacrimal gland, often with stranding of the surrounding orbital fat. Bony erosion is absent. Contrast enhancement is seen acutely (Vaidhyanath et al. 2008).

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Differential Diagnosis

Ruptured dermoid
Hordeolum
Preseptal cellulitis (with or without abscess)
Orbital cellulitis
Lacrimal gland tumor (Hayek and Esmaeli 2006)
Metastatic orbital disease

Therapy

A short course of oral antibiotics is often administered along with warm compresses and NSAIDs. Cephalexin is a popular initial agent. The majority of cases in children are viral and improve with supportive care alone. Oral corticosteroids are the first-line therapy for IOI. Steroid-sparing agents may be used for failures and relapses. Therapy for cases associated with systemic disease is directed toward the underlying condition.

Prognosis

Prognosis for acute dacryoadenitis is generally excellent. For chronic dacryoadenitis, prognosis depends on control of the underlying condition.

Epidemiology

Dacryocystitis is relatively rare and there are no reliable estimates of incidence in the literature. Apart from specific subsets, there is no known predilection based on gender or race. Age of onset is highly variable. IOI-associated dacryoadenitis may be seen in children as young as 3 years of age.

Cross-References

► Cellulitis, Preseptal, Haemophilus Causing
► Sarcoidosis

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Dacryoadenoma

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Synonyms

Conjunctival epithelial tumor

Definition

A rare conjunctival tumor that presents as a pink mass in the inferior bulbar or palpebral region.

Etiology

This is a benign tumor that appears to originate from metaplasia of the surface epithelium and proliferates into the stroma (Yanoff and Sassani 2008).

Clinical Presentation

Dacryoadenoma is a rare conjunctival tumor that is found in children or young adults. It is not known if it is congenital or acquired, as there has been very

few case reports ever described. One case was noted in a 33-year-old patient who had the inferior fornix lesion removed when she was 48 (Jakobiec et al. 1989). It was unknown if she had the lesion since birth. In another case, the lesion was on the bulbar conjunctiva of a 14-year-old girl (Shields and Shields 2008). It was noted to be a darker red mass on the bulbar conjunctiva, which slowly enlarged over time. This benign tumor originates from the surface epithelium and proliferates into the stroma where it forms glandular lobules similar to the lacrimal gland.

Diagnostics

Rarely suspected on clinical exam.

Histopathology: Metaplasia of the conjunctiva epithelium with invagination into the underling stroma, forming tubules and glands.

Electron microscopy: Presence of zymogen-type lacrimal secretory granules.

Differential Diagnosis

Differential diagnosis includes lymphoma and other pink- or salmon-colored masses in the conjunctiva.

Prophylaxis

None

Therapy

Careful monitoring
Excisional biopsy

Prognosis

Excellent

Epidemiology

Children and young adults

Cross-References

▶ Conjunctival Tumors
▶ Lymphoma: Definition

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Dacryocystitis

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Definition

Dacryocystitis is a bacterial or fungal infection of the nasolacrimal sac, which results from an obstruction of the nasolacrimal duct and stasis of tears in the lacrimal drainage system.

Etiology

Dacryocystitis may develop at any age, but it occurs more commonly in infants, young adults, and the elderly. Infantile dacryocystitis may result from incomplete canalization of the nasolacrimal duct, nasolacrimal atresia, facial cleft, and dacryocystocele (Tower 2008). Simple congenital nasolacrimal duct obstruction secondary to incomplete nasolacrimal duct canalization at the level of the valve of Hasner is more common than congenital dacryocystocele. Dacryocystocele is a distended noninfected lacrimal sac, which may be present at birth due to amniotic fluid entering and

obstructing the nasolacrimal sac. Few of the infants affected by dacryocystocele go on to develop acute infections. Acquired causes of obstruction include trauma, gradual narrowing over time, dacryolith, tumor impinging on sac or duct, granuloma, foreign body, or result of previous infections (Tower 2008; Jordan 2011). Young adults commonly develop dacryocystitis secondary obstruction from trauma or a dacryolith (Jordan 2011). A tumor intrinsic to the lacrimal sac or extrinsic and impinging on the sac or duct may cause an obstruction. A retained foreign body, such as from a prior lacrimal intubation, may also be a cause (Tower 2008). Obstruction causes accumulation of microorganisms and cellular debris in the nasolacrimal sac with the potential for development of an infection. Upper respiratory tract organisms such as β-hemolytic Streptococcus or Staphylococcus are common etiologic organisms (Jordan 2011).

Clinical Presentation

Acute dacryocystitis has a rapid onset. There are also chronic and subacute forms of dacryocystitis. There is often redness, tenderness, and swelling that is inferior to the medial palpebral ligament. Pain is often intense and is due to distension of the nasolacrimal sac (Jordan 2011).

The infection can spread and become cellulitis of the eyelid and orbit or become an abscess (Hurwitz 2014; Jordan 2011). This may cause swelling of the eyelids to be prominent at presentation. With massaging of the lacrimal sac, mucopurulent discharge can reflux through the canaliculus (Coats 2008; Tower 2008). Because of the obstruction, there often is overflow tearing and an increased tear lake (Coats 2008).

Epiphora and mattering of the eyelids may be a sign of congenital nasolacrimal obstruction in infants. Symptoms present within the first 6 weeks of life and may also be accompanied by chronic mucopurulent discharge from one or both eyes (Tower 2008). Important to note is the lack of conjunctival erythema.

Chronic dacryocystitis tends to be indolent, presenting with tearing and mild to moderate recurrent unilateral discharge. Applying pressure over the nasolacrimal sac may produce a reflux of mucoid or mucopurulent discharge from the punctum (Jordan 2011). Various bacteria may be involved, the most common of which are *Staphylococcus aureus*, *Streptococcus* species, and *Escherichia coli* (Durand 2010). Other pathogens include other *Staphylococcus* species; Gram-negative bacteria, including *Haemophilus influenzae*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*; and anaerobic bacteria, such as *Arachnia propionica*. Rarely, *Mycobacterium tuberculosis*, *Chlamydia trachomatis*, and fungi, such as *Candida*, *Aspergillus niger*, and *Pityrosporum*, may be involved. Complications of chronic dacryocystitis include acute recurrent dacryocystitis, infectious keratitis, and endophthalmitis following corneal trauma or intraocular surgery (Jordan 2011). Patients may also develop a dacryocutaneous fistula following cases of spontaneous rupture (Tower 2008).

Diagnosis

Typically diagnosis is based on clinical presentation. Infantile dacryocystitis may be diagnosed by classic symptoms of epiphora and discharge in the absence of conjunctival erythema (Tower 2008). Acquired acute dacryocystitis is typically a clinical diagnosis (Jordan 2011). Digital pressure or massage over the lacrimal sac may result in reflux of mucopurulent material. Cultures are sent to determine the organism and appropriate antibiotic therapy. Another test that may be useful is the fluorescein dye retention test to determine if the lacrimal drainage is poor as expected with obstruction (Coats 2008; Tower 2008). While not often needed, dacryocystography can be useful in determining the site of stenosis or obstruction (Hurwitz 2014).

Differential Diagnosis

The differential diagnosis for infantile dacryocystitis includes simple congental obstruction secondary to incomplete canalization of the nasolacrimal duct, punctal or canalicular atresia,

conjunctivitis, conjunctival foreign body, nasal mucosal edema, and orbital cellulitis (Tower 2008). Simple congenital obstruction secondary to incomplete canalization and atresia may manifest as epiphora and mattering of the eyelids. Additionally, they may present with minimal dilation of the lacrimal sac. This condition is benign, but must be distinguished from acute dacryocystitis (Jordan 2011). Conjunctivitis causes the conjunctiva to appear red and typically responds to topical antibiotics. Conjunctival foreign body typically presents as an acute onset red eye. Nasal mucosal edema results in tearing secondary to inferior meatus obstruction, and it typically resolves with decongestants (Tower 2008). Dacryocystitis may be mistaken for orbital cellulitis in newborns and infants. It is preferable to hospitalize these patients and initiate therapy with intravenous antibiotics to prevent orbital abscess or sepsis (Jordan 2011).

Punctal or canalicular stenosis and conditions causing impairment of the lacrimal pump must be ruled out when a diagnosis of acquired and chronic dacryocystitis is considered. In cases of stenosis, patients present with epiphora without mucus. Obstruction of the upper canalicular system may be revealed by probing and irrigation. Epiphora may result from conditions leading to a poor lacrimal pump function, such as cranial nerve VII palsy, eyelid deformity impairing lid movement, senile eyelid laxity, and flaccidity (Tower 2008).

Prophylaxis

With congenital dacryocystocele, there is controversy, but some clinicians start with antibiotics and massage (Jordan 2011). If it fails to resolve, the dacryocystocele may be surgically treated using endoscopically guided marsupialization of the dacryocystocele and stenting the nasolacrimal system (Jordan 2011). Prophylaxis for acquired forms of dacryocystitis is unclear.

Therapy

With infants and younger children, they should be hospitalized for intravenous broad-spectrum antibiotics empirically until culture results indicate a narrow spectrum antibiotic (Jordan 2011; Tower 2008). Treatment is important and can be life threatening in infants and young children.

Congenital obstruction typically resolves spontaneously, but probing by passing a probe into the lower canaliculus and up through the nose is the first intervention (Hurwitz 2014). This is typically successful with a 90% success rate (Tower 2008). If this fails, silastic tubes for 3–6 months are often tried, and then if this too fails, dacryocystorhinostomy is performed, but this is rarely needed (Tower 2008; Hurwitz 2014).

For all forms, warm compress and pain relief can help the symptoms of dacryocystitis. The main goal of therapy is to treat the infection. Topical and systemic antibiotics are used first. If there is no improvement in 48–72 h, intravenous antibiotic therapy should be started (Jordan 2011). If postseptal orbital cellulitis is suspected, a CT scan should be ordered to look for abscesses in which intravenous antibiotics are indicated (Hurwitz 2014). If a superficial fluctuant mass is present, a stab incision to drain is part of therapy (Jordan 2011). A dacryocystotomy is reserved for when infection continues to persist and perforation is impending (Hurwitz 2014). Probing may be used to drain the lacrimal sac by inserting a probe through the canaliculus until the sac contents empty into the conjunctiva (Tower 2008). Chronic forms require treatment with antibiotics and digital decompression until surgical intervention (Tower 2008).

Surgical treatment for adults includes external dacryocystorhinostomy, endonasal endoscopic dacryocystorhinostomy, or balloon catheterization (Tower 2008). Balloon catheterization is less studied but has shown promise in some reports (Tower 2008; Coats 2008). External dacryocystorhinostomy has a 95% success rate when done by experienced surgeons (Tower 2008).

Prognosis

Most infants experience spontaneous resolution of dacryocystitis within the first 6 months of life.

More than 90% outgrow the condition by 1 year. With proper therapy, acute dacryocystitis resolves within 7–14 days (Tower 2008). Acute dacryocystitis may spread to the anterior orbit, resulting in significant swelling of the eyelid, or the posterior to the orbital septum, producing orbital cellulitis with complications of globe displacement, afferent pupillary defect, optic neuropathy, and visual loss. Of patients with an initial attack of acute dacryocystitis, 60% will experience a recurrence (Hurwitz 2014).

In patients requiring incision and drainage for a lacrimal abscess, approximately 8% will require a repeat procedure. One study found that 25% of patients with a lacrimal sac abscess who did not undergo definitive surgical treatment with dacryocystorhinostomy or dacryocystectomy developed a recurrent lacrimal sac abscess (Durand 2010). When dacryocystorhinostomy is required, it is reported to have a success rate of 95% when performed by experienced surgeons (Tower 2008).

A common complication of not treating dacryocystitis is rupture through the skin causing a dacryocutaneous fistula (Tower 2008). Complications can include infectious dermatitis, endophthalmitis, and acute recurrent dacryocystitis (Jordan 2011). Unfortunately, recurrent attacks are not uncommon and can occur in 60% of patients.

Epidemiology

Congenital forms are present in 2–6% of live births (Coats 2008; Tower 2008). Acquired forms are most common in certain age groups including mid-30s and older than 65 (Jordan 2011). Young women are the most likely to have dacryoliths, which is the most common form of acquired dacryocystitis (Tower 2008; Jordan 2011).

Cross-References

► Conjunctivitis
► Tearing (Epiphora)

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DALK

► Transplantation

Daltonism

► Achromatopsia Cerebral

Darier Disease (Keratosis Follicularis)

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Synonyms

Darier-White disease; Dyskeratosis follicularis

Definition

Keratosis follicularis is a genodermatosis characterized by abnormal keratinization of the epidermis, nails, and mucous membranes.

Etiology

Keratosis follicularis is an autosomal dominant disorder caused by mutations in the ATP2A2 gene, which encodes the Ca^{2+} ATPase 2 isoform. This defect results in disturbed cell-to-cell adhesion and differentiation of the epidermis (Ringpfeil et al. 2001).

Clinical Presentation

Clinical features consist of disseminated warty papules and plaques with an affinity for the seborrheic areas of the body including the face, scalp, and upper trunk (Sehgal and Srivastava 2005).

Ocular involvement in keratosis follicularis is relatively uncommon. Eyelid manifestations parallel cutaneous findings and are characterized by warty hyperkeratotic plaques with accumulation of seborrhea-like debris at the eyelid margin. Most of the affected patients have dry eye syndrome with and without Sjögren's syndrome (Mielke et al. 2002). Possible corneal manifestations are peripheral arcus lipoides-like opacifications, asymptomatic nebular dot-like opacities of the peripheral corneal epithelium, and central epithelial surface irregularities.

Diagnostics

Histopathologic examination of the peripheral corneal lesions shows corneal edema and separation of the basal epithelium of Bowman's layer by granular material. Electron microscopy has shown this granular material to represent remnants of cell debris and an electron-dense granular substance (Blackman et al. 1980).

Clinical diagnosis can be confirmed by biopsy. Histopathologic findings of cutaneous lesions include dyskeratosis represented by eosinophilic corps rounds and grains and acantholysis with suprabasal intraepidermal cleavage. These cutaneous lesions are histopathologically different from corneal lesions as the cornea is not normally a keratinizing epithelium (Daicker 1995).

Differential Diagnosis

The differential diagnosis for keratosis follicularis includes other genodermatoses with corneal changes including keratosis plantaris, Kyrle disease, and tyrosinemia. Anterior basement membrane dystrophy and Salzmann's nodular degeneration may be included in the differential for the peripheral corneal opacities found in keratosis follicularis (Blackman et al. 1980).

Prophylaxis

Uncertain

Therapy

Keratosis follicularis may result in reduced corneal protection and microbiological colonization which may lead to recurrent corneal ulcerations. Along with long-term dermatological medical care, intensive ocular therapy with lubricants with the consideration of antibiotics is recommended (Mielke et al. 2002).

Prognosis

Uncertain

Epidemiology

The incidence varies from 1:30,000 to 1:100,000, with an average age of onset in the first or second decade.

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Darier-White Disease

▶ Darier Disease (Keratosis Follicularis)

Dark Adaptation Testing

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Synonyms

Dark adaptometry

Definition

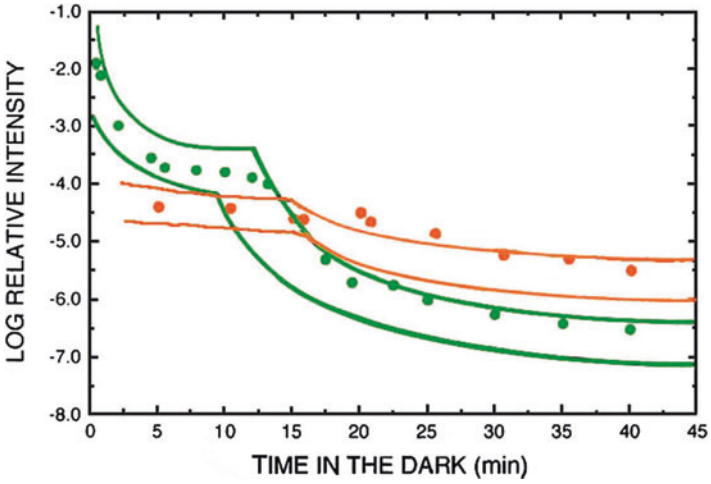
A test for monitoring time-dependent changes in retinal sensitivity to light stimuli when moving from a bright light environment to darkness.

Purpose

To evaluate the rate at which sensitivity to light stimuli of the "cone system" and of the "rod system" recover when ambient illumination is changed from bright light to darkness. *The terms "cone system" and "rod system" refer respectively to the cones and rods, each class of photoreceptors has its own associated neural network in the retina, conveying signals to the brain in order to elicit visual perception.

Principle

Dark adaptation test is a psychophysical test in which patient cooperation is mandatory. The patient is required to fixate the tested eye (the non-tested eye is covered with an eye patch) to a red fixation light, while a flickering (typically 1 Hz) test light field is modulated in intensity. The task of the patient is to signal the detection of the flickering test light. The testing procedure usually starts with a learning phase in which the patient becomes acquainted with the setup and with his/her task. Then, the patient is instructed to fixate at a bright light source for about 3 min in order to bleach at least 80% of rhodopsin, the visual pigment of the rod photoreceptors. Cones' visual pigments are bleached too but to a lesser extent. Following the bleaching exposure, the actual dark adaptation test starts, and threshold for detecting the flickering test light is measured periodically. For threshold determination, the intensity of the flickering test light is lowered to levels that cannot be detected, and the patient is asked to fixate on the red fixation light while the intensity of the flickering light is gradually increased until the patient signals its detection. The intensity at which the flicker was detected is the threshold for that period of time in darkness. In the complete test, thresholds are determined during 2 h in darkness after the bleaching; however it is usually sufficient to follow only the first 40 min since sensitivity recovery is close to 99% complete. In order to determine which visual component, the cone system or the rod system determine visual sensitivity during the dark adaptation process, it is advised to use intermittently green (500 nm) light and orange (600 nm) light for the flickering test light as illustrated in Fig. 1. The cone system is more sensitive to the 600 nm light compared to the 500 nm light, while the rod system is more sensitive to the green light compared to the red light. A clear change from cone-mediated vision to rod-mediated vision is seen at 8–10 min in darkness.



Dark Adaptation Testing, Fig. 1 Normal dark adaptation curve after a substantial bleaching of rhodopsin (at least 75%), using green (500 nm) and orange (600 nm) test lights. The two continuous lines mark the normal spread of 20 volunteers with normal vision. The data points show results of a patient with normal dark adaptation

The size of the flickering test light may vary in dimension but has to stay fixed throughout the test. A field of 2° in diameter is usually used. Another important parameter that needs to be considered is the retina region that is illuminated by the flickering test light. Usually, a region located 15–20° from the fovea is used, since this locus contains the highest density of rod photoreceptors. However, other loci may be considered depending upon the patient complaint and medical history. In order to get reproducible test results, it is important to standardize the test procedure and parameters.

Figure 1 shows the range of dark adaptation for 20 volunteers with normal day- and night-vision (continuous curves) and data from one subject who complained of visual difficulties at night (red and green data points) and was found to have normal dark adaption curve. The first 6–7 min after bleaching reflects sensitivity recovery of the cone system, which stabilizes after about 6–8 min. This is a relatively fast sensitivity recovery phase, and it is beneficial to measure threshold every 30 s. At around 10 min following termination of the bleaching exposure, a second phase of sensitivity increase is detected, the recovery of the rod system. This lasts for another 20–25 min and stabilizes after about 35–40 min in darkness. Separation between dark adaptation of the cone system and that of the rod system can be done by asking the patient if she/he sees color when detecting the flickering light; during the recovery of the cone system, the patient can easily identify the color of the stimulus, while during the rod recovery phase it appears gray. As shown in Fig. 1, when intermittent green (500 nm) light and orange (600 nm) light are used for the flickering test light, two components can easily be identified in the dark adaptation curve, reflecting recovery of the cone system and of the rod system. Since the total range of visual sensitivity recovery from immediately after the bright light exposure to complete dark adaptation is very large, in the order of 100,000-fold, threshold is given in log units in the ordinate of the dark adaptation curve (Fig. 1).

Indication

Evaluation of visual function at night: The dark adaptation test is used to complement the electroretinogram (ERG) test in patients complaining of difficulties in night vision. Regardless of the results of the dark-adapted ERG responses, psychophysical testing of dark adaptation is recommended because it is more quantitative in determining the magnitude of difficulty in night vision compared to the ERG recording and because discrepancies between ERG findings and dark adaptation may be seen in several settings including Duchene Muscular Dystrophy and Dominant Electronegative ERG.

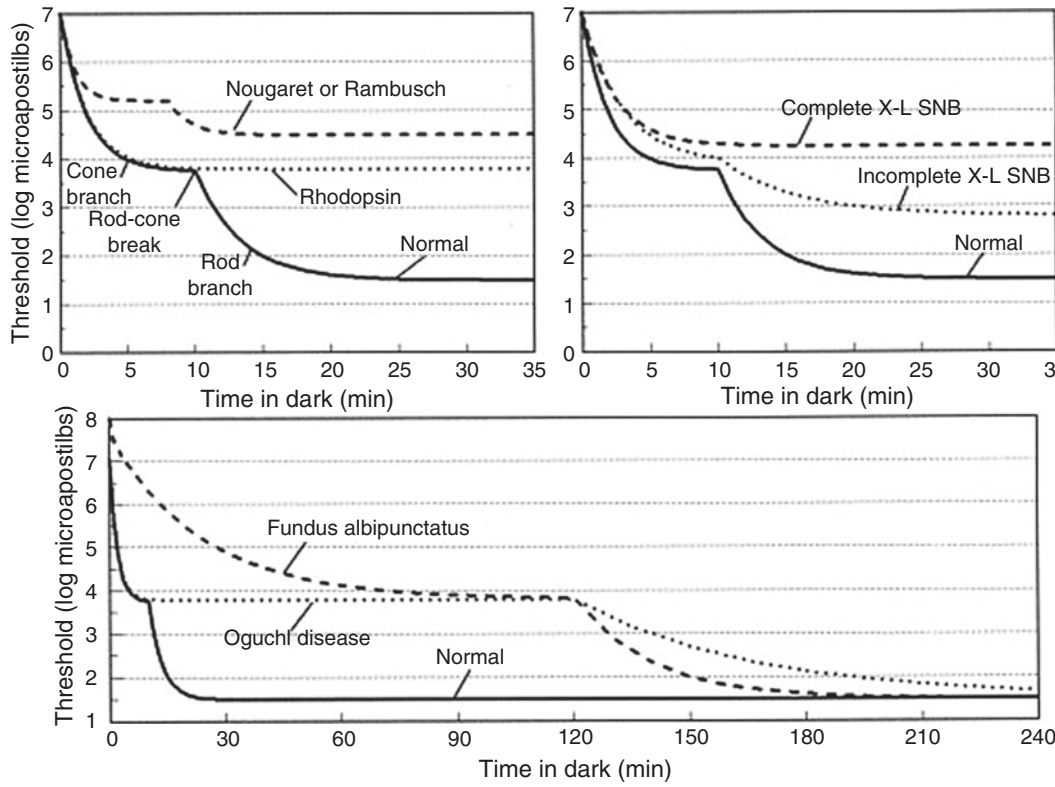
Suspected inherited stationary disorder in night vision: Inherited stationary disorders in night vision

reflect mutation in genes coding for proteins participating in the rhodopsin cycle or proteins associated with the rod system in the retina. These cases are associated with typical changes in the ERG responses, but for quantitative assessment of night vision and for exact determination of the type of disorder, dark adaptation test is recommended, as illustrated for a few typical cases in Fig. 2 (Dryja 2000).

The dark adaptation curve found in incomplete x-linked congenital stationary night blindness (CSNB) demonstrates a slight reduction in the rate of cone system recovery, a normal timing of rod system-cone system break, and a reduction in the rate of rod system recovery with final dark adapted thresholds higher than normal, but the rod system dominates light detection. In contrast, in the complete form of CSNB, the dark adaptation curve shows only a cone system component of elevated threshold compared to the normal, but there is no rod system recovery and vision is controlled by the cone system.

In other two types of congenital difficulties in night vision, shown in Fig. 2, the rate of dark adaptation is delayed, but final threshold is normal. In fundus albipunctatus, sensitivity recovery of the cone system and of the rod system are considerably delayed, but after sufficient time in the dark, the sensitivity to light of the rod system is normal. In contrast, patients with Oguchi disease, show normal recovery of the cone system, but delayed recovery of the rod system. In patients with Oguchi disease, normal sensitivity to light of the rod system is reached if they stay in darkness for sufficiently long period of time.

Vitamin A deficiency: Patients suffering from vitamin A deficiency from any underlying cause



Dark Adaptation Testing, Fig. 2 Representative dark-adaptation curves of patients suffering from different genetic source leading to night vision deficiency. (Dryja 2000)

should be tested for dark adaptation because difficulties in night vision start relatively late after vitamin A deficiency starts. In the western world, cases of vitamin A deficiency due to malnutrition are rare, but other causes for vitamin A deficiency, including liver cirrhosis, bariatric surgery and extreme weight losing diets, increase in number.

Contraindication

Non cooperating patient

Advantage/Disadvantage

Advantage: physiologic, quantitative and functional assessment of night blindness. May be used to follow up on disease progression and response to treatment.

Disadvantage: lengthy process that requires patient cooperation.

Cross-References

- ▶ Congenital Color Vision Defects
- ▶ Electroretinogram
- ▶ Fundus Albipunctatus

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Dark Adaptometry

- ▶ Dark Adaptation Testing

Day Blindness (Hemeralopia), in Cone Dystrophies

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D

Synonyms

Heliophobia; Photophobia

Definition

Day blindness (hemeralopia) is a symptom in which vision is impaired in daytime (photopic conditions), whereas night vision (scotopic conditions) is preserved.

Etiology

The visual system consists of two components that are relatively independent of one another. One component is responsible for vision in daytime, the photopic system, which is based upon the cone photoreceptors. The other component is responsible for vision under dark conditions, the scotopic system, which is based upon the rod photoreceptors. There is a slight overlap between the two systems during dim background illumination (mesopic conditions), but in general, rods cannot replace cones for daytime vision and cones cannot replace rods for night vision.

Difficulties in day vision, ranging from slight photophobia to day blindness, can result from any condition in which cone photoreceptor function is diffusely impaired, or from conditions in which too much light enters the ocular globe.

1. Cone dystrophy, cone-rod dystrophy, and achromatopsia (inherited disorder of complete

absence of functioning cones in the retina) can lead to difficulties in visual function during bright ambient illumination, resulting in day blindness and photoaversion.

In contrast, ocular conditions affecting only macular cone photoreceptors such as inherited macular degeneration (Stargardt's disease, best vitelliform macular dystrophy) and age-related macular degeneration will not typically cause hemeralopia, as functionally preserved peripheral cones can light adapt when ambient illumination increases.

2. Other conditions potentially associated with aversion from bright light include conditions in which intraocular light dispersion occurs, such as ocular albinism, central cataract, corneal abrasion, aniridia, anisocoria, and a tonic pupil (Adie's pupil) in which pupillary constriction in response to light is inadequate.

Occurrence

It cannot be specified because it changes according to the diversity of pathologies causing hemeralopia (photophobia) and the variability of each of these causes in different populations.

Cross-References

- ▶ Adie's Pupil
- ▶ Albinism
- ▶ Aniridia, Traumatic
- ▶ Anisocoria
- ▶ Cone-Rod Dystrophy
- ▶ Rod-Cone Dystrophy

Decentration

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Synonyms

Off-center optics

Definition

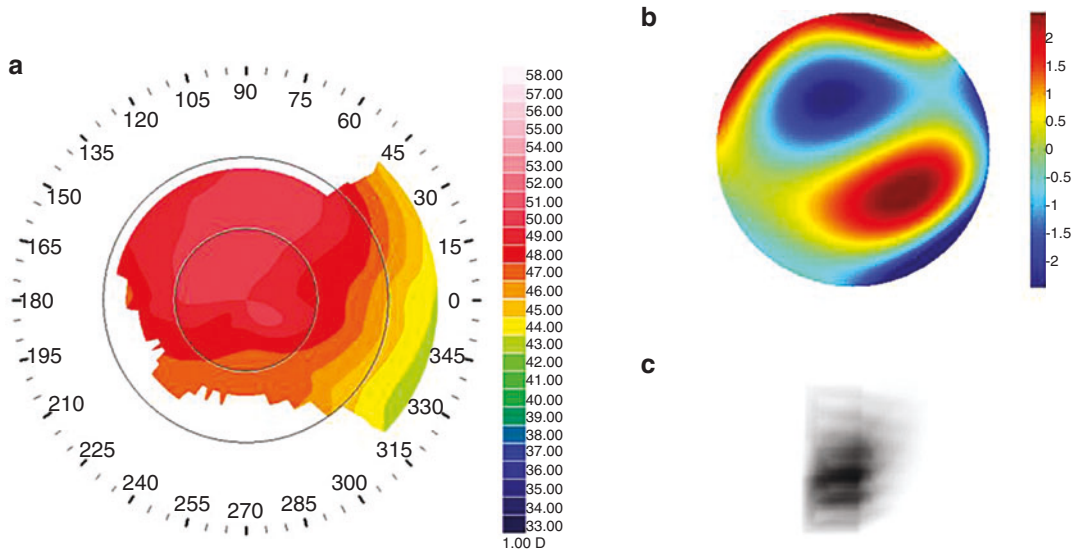
Misalignment of an optical component relative to the reference axis. In geometric optics, the misalignment can be a shift or tilt relatively to the optical axis, or a combination of both. In ophthalmic optics, the term "decentration" refers to the shift of the crystalline lens, an intraocular lens (IOL), a corneal refractive treatment, a contact lens, or the lens in a frame relatively to the visual axis. Decentration of the pupil is called korectopia.

History

From the construction of optical systems and from the introduction of glasses it became evident that for an optimum image quality the components of an optical system need to be aligned along a reference axis. Phoropters were equipped with centration crosses to ensure proper alignment during the process of subjective refraction. The introduction of IOL implantation and excimer laser corneal refractive surgery in ophthalmology brought the problem of tilt and decentration into the focus of ophthalmic surgeons and ophthalmic research.

Clinical Features

A tilted optical system causes a prismatic effect (tilt) while decentration by shift induces astigmatism (of oblique bundles) and higher-order aberrations (HOA), mainly coma. Coma is typically induced if spherical aberration is present. Patients then often complain about a ghost image or "shadow." The clinical symptoms are highly dependent of the amount of decentration and the power of the decentered optical system. A decentration of a spherical IOL of less than 500 µm might be asymptomatic (Baumeister et al. 2009). In contrast, a decentration of a corneal excimer ablation of −12 D with a small optical zone over the same range – as it was common in the early days of excimer laser refractive surgery – can cause significant symptoms due to



Decentration, Fig. 1 Decentered hyperopic LASIK ablation. **A**, corneal topography **B**, wavefront map **C**, simulation

coma induction. Simulation studies showed that the effects of decentration on retinal image quality are more pronounced if spherical aberration is introduced and the pupil diameter is large (Bühren et al. 2007; Bühren et al. 2010b). Consequently, aspheric ablation profiles that introduce less spherical aberration are more tolerant to decentration (Bühren et al. 2010a).

Tests

The diagnostic procedure is dependent from which optical component is assumed to be decentered. A grossly decentered (subluxated) IOL or LASIK flap can be seen at the slit-lamp. Quantification of IOL tilt and decentration can be achieved by Scheimpflug photography, optical coherence tomography, or with a Purkinje meter. In case of decentered corneal excimer ablation (Fig. 1), corneal topography can reveal the decentration. Aberrometry is capable of quantification of coma, spherical aberration, and other HOA of the whole eye. Devices that combine topography and aberrometry are the ideal tools for separating HOA originating from the cornea and the lens or IOL.

Differential Diagnosis

Because the symptoms of decentration-induced HOA are similar regardless of the origin of decentration, the first step involves the differential diagnosis between corneal and lenticular aberrations or even aberrations due to a misaligned lens in a frame of glasses. Other differential diagnoses include corneal scars, keratoconus (which could be considered as a decentered optical system sui generis), and cataract.

Etiology

Decentration of a corneal laser treatment occurs if the treatment is misaligned relative to the visual axis. This can either happen due to a primary misalignment (failure to center the treatment correctly) or as secondary decentration due to shift during the treatment. The introduction of eye trackers that compensate for eye movements during the process of treatment has increased alignment precision. The correct initial alignment relative to the optical axis is achieved by a fixation laser beam that visualizes the patient's visual axis to the surgeon. Decentration of IOLs occurs

typically in case of poor capsular or zonular support, decentered capsulorrhexis, asymmetric shrinkage of the capsular bag, misplacement of the haptics, and misalignment of an iris-supported IOL relatively to the pupil. A recently more prevalent problem is the late (sub-) luxation of IOLs implanted in the capsular bag in eyes with pseudoexfoliation.

Treatment

For a decentered corneal refractive treatment (ablative, incisive, or coagulative), the most efficient treatment is the correction of HOA by a rigid contact lens which is, however, seldom tolerated in refractive patients. Another, yet not always effective, option to reduce HOA is topography-guided excimer surgery. An IOL subluxated with the capsular bag that causes symptoms can be either recentered (e.g., using a Cionni ring) or can be replaced by an iris-fixated IOL.

Very important is the prophylaxis of decentration: a correct centration of the ablation to the visual axis, a centered capsulorrhexis in cataract surgery, and in case of sulcus implantation of IOLs an anterior optic capture.

Prognosis

In case of decentered corneal refractive treatment, there is no progression to be expected. Decentration of IOLs due to zonular weakness in pseudoexfoliation syndrome is likely to increase over time. In terms of vision, prognosis is good, if a rigid contact lens can be fitted or if the IOL can be recentered or replaced.

Cross-References

- ▶ Aspheric Ablation Profile
- ▶ Coma
- ▶ Excimer Lasers
- ▶ Higher-Order Aberrations, Refractive Surgery
- ▶ IOL
- ▶ Photorefractive Keratectomy (PRK)

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Decoagulants

▶ Anticoagulants, Ophthalmological Treatment

Deep Anterior Lamellar Keratoplasty (DALK)

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Synonyms

Descemet's deep anterior lamellar keratoplasty; Maximum depth deep anterior lamellar keratoplasty; Predescemet deep anterior lamellar keratoplasty

Definition

Deep anterior lamellar keratoplasty (DALK) is a surgical procedure in which diseased corneal stroma is replaced by donor tissue, preserving host Descemet's membrane and endothelium.

Indications

DALK is the corneal transplant procedure of choice for patients harboring diseases of corneal stroma but normal Descemet's membrane and endothelium. Indications include ectatic disorders (keratoconus, keratoglobus, pellucid marginal degeneration, post-refractive ectasia), corneal scars, and anterior corneal dystrophies. DALK may be preferred over penetrating keratoplasty in monocular or noncompliant patients.

Compared to penetrating keratoplasty, DALK may result in better long-term graft survival, less dependency on steroids, earlier suture removal, less stringent follow-up and donor tissue requirements, and decreased graft rejections. Although penetrating keratoplasty may be efficacious, DALK is becoming the procedure of choice for corneal stromal diseases.

Contraindications

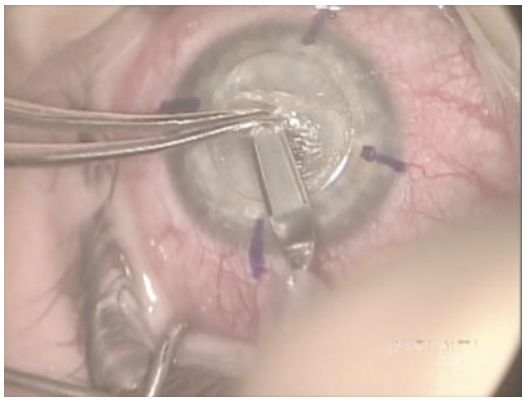
DALK is contraindicated in any condition in which Descemet's membrane or endothelium is unhealthy, including corneal hydrops or Descemet's scarring.

Techniques and Principles

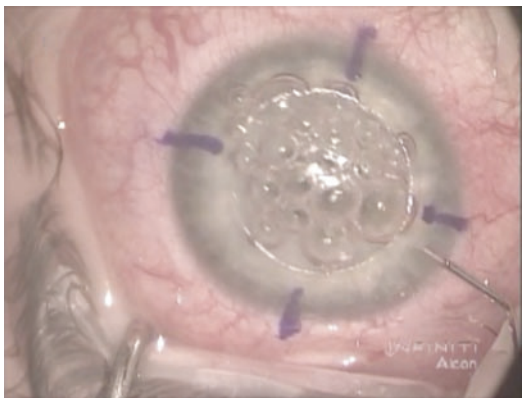
Achieving optimal visual results with DALK depends on the smoothness of the graft-donor interface and deepness of dissection. The big-bubble technique, described by Anwar and Teichman, achieves these two principles, making it the most popular DALK technique among cornea surgeons worldwide.

The big-bubble technique involves the following steps:

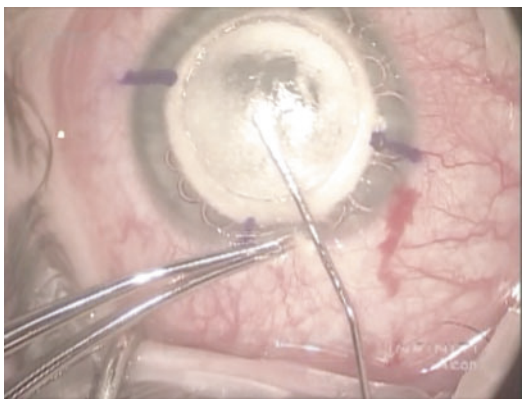
1. Trephination of the central host cornea with or without lamellar dissection, depressurization of the anterior chamber, and injection of small air bubbles in the anterior chamber (see Figs. 1 and 2)
2. Stromal delamination with the big-bubble formation (see Fig. 3)



Deep Anterior Lamellar Keratoplasty (DALK), Fig. 1 Lamellar dissection



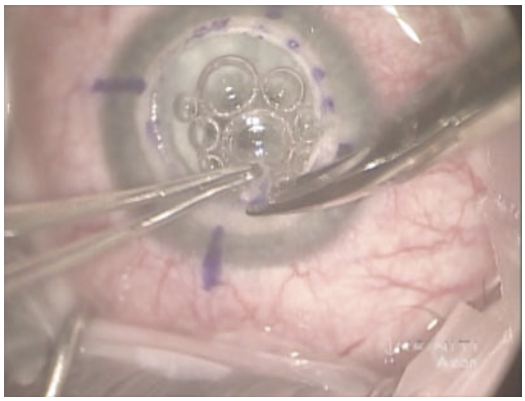
Deep Anterior Lamellar Keratoplasty (DALK), Fig. 2 Depressurization and injection of air bubbles in the anterior chamber



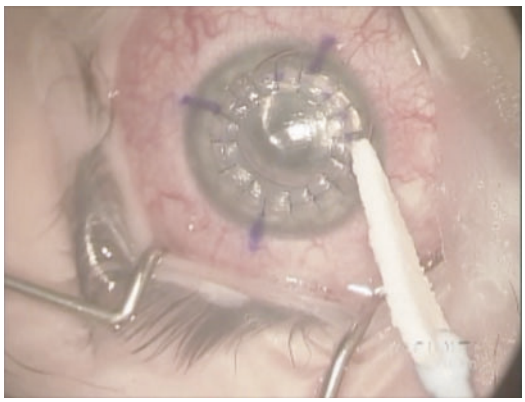
Deep Anterior Lamellar Keratoplasty (DALK), Fig. 3 Stromal delamination with big-bubble formation

(a) Air is injected intrastromally through a small-bore needle or cannula creating a separation between the stroma and Descemet's membrane.

3. Removal of residual stroma and baring of Descemet's membrane (see Fig. 4)
   (a) Small incision is made in the posterior stroma, and the big-bubble plane is entered.
   (b) Gentle dissection is performed if necessary, often with the aid of viscoelastic.
   (c) Dissected stroma is removed using blunt-tipped scissors.
4. Donor tissue preparation and placement into lamellar bed (see Fig. 5)



Deep Anterior Lamellar Keratoplasty (DALK), Fig. 4 Removal of residual stroma



Deep Anterior Lamellar Keratoplasty (DALK), Fig. 5 Donor tissue placement into lamellar bed

Other described DALK techniques include manual lamellar dissection and automated lamellar keratoplasty.

Outcome

Penetrating keratoplasty is the standard against which deep lamellar keratoplasty has been compared in terms of outcomes. The interface between the host and donor tissues has been postulated to be a possible cause of decreased visual acuity in DALK. Due to the increased popularity of lamellar procedures in recent years, several studies have compared DALK and penetrating keratoplasty in terms of visual outcomes, endothelial cell loss, graft survival, and resistance to trauma.

In terms of visual outcomes, DALK is at least equally effective in restoring vision compared with penetrating keratoplasty. Deep dissections baring Descemet's membrane must be achieved in order to obtain visual results comparable to full-thickness corneal transplants.

Uncomplicated DALK cases have less endothelial cell loss than the traditional penetrating keratoplasty. Cases in which Descemet's membrane has been perforated have the same rate of endothelial cell loss as in full-thickness transplants.

Studies have demonstrated graft survival is higher in lamellar procedures, mainly due to decreased endothelial cell loss and decreased rates of rejections.

Theoretically, lamellar corneal transplants have greater resistance to trauma compared to penetrating keratoplasty. There are several reports of traumatic wound dehiscence after DALK in the literature.

Based on the evidence we have, DALK should be the procedure of choice in diseases affecting corneal stroma.

Complications

The most common intraoperative complication in DALK is rupture of Descemet's membrane. It may be violated during trephination, stromal dissection, and passing a suture needle. Care must be

taken during these three steps. In the event of a big rupture, case must be converted into a penetrating keratoplasty.

Postoperative complications unique to DALK include papillary block, pseudoanterior chamber, Urrets-Zavalia syndrome, and post-keratoplasty atopic sclerokeratitis.

Cross-References

- ▶ Ectasia, Corneal
- ▶ Endothelial Graft Rejection
- ▶ Hydrops, Keratoconus
- ▶ Keratoconus
- ▶ Keratoglobus
- ▶ Lamellar Keratoplasty
- ▶ Stromal Dystrophies

Further Reading

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Deep Lamellar Endothelial Keratoplasty (DLEK)

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Synonyms

Posterior lamellar keratoplasty

Definition

Deep lamellar endothelial keratoplasty (DLEK) is a procedure that involves the selective transplantation of components of the cornea. DLEK is performed through the limbal scleral incision, leaving the corneal surface of the recipient untouched. In 1998, Gerrit Melles, MD, of the Netherlands laid the foundation of modern endothelial keratoplasty in a procedure he termed posterior lamellar keratoplasty (PLK). He was the first surgeon to perform an endothelial keratoplasty using a scleral limbal approach in a human (Shamie et al. 2009). The technique that Melles utilized in PLK involved dissection of the posterior lamella, Descemet's membrane, and the endothelium through a 9.0 mm sclerocorneal incision, and grafting of a donor disk of these three layers. The graft is held in place by an air bubble while the patient lies supine (Fernandez and Afshari 2010). Melles utilized air for resection of the recipient tissue and stabilization of the donor graft after insertion. Additionally, this technique obviated the need for corneal sutures (Shamie et al. 2009).

Melles named the procedure posterior lamellar keratoplasty, which was the same name utilized by surgeons performing endothelial keratoplasty under a hinged flap in the past (Shamie et al. 2009). Melles later revised the procedure using a 5.0 mm incision and bending the graft tissue to allow for insertion. This revision resulted in rapid improvement in visual acuity with only a small increase in astigmatism at 6 months postoperatively. However, the procedure was technically difficult, and it required the manual dissection of both donor and host stromal beds (Fernandez and Afshari 2010).

In the United States, Mark Terry, MD, adopted the PLK procedure and termed it deep lamellar endothelial keratoplasty. Terry worked to simplify the procedure, using a cohesive viscoelastic agent to stabilize the anterior chamber (Fernandez and Afshari 2010). When Terry adopted the PLK procedure, he worked on simplifying the procedure while maintaining or improving its results. He used Healon, a cohesive viscoelastic agent, to stabilize the anterior chamber. The cohesive characteristics of Healon allowed it to be easily removed in its entirety without residual coating of the tissue and without hindering the donor graft adhesion. He renamed the procedure deep lamellar endothelial keratoplasty to differentiate it from the posterior lamellar keratoplasty procedure used

in the past, which involved the creation of a hinged corneal flap, and to emphasize the endothelial transplantation involved in the procedure (Shamie et al. 2009). This procedure was technically difficult, but its development led to an accelerated movement of advancements in endothelial keratoplasty (Fernandez and Afshari 2010).

In endothelial keratoplasty, only a portion of the recipient's posterior cornea is removed and a small graft is transplanted in its place. By grafting only a portion of cornea, less foreign antigen is introduced to the donor. Additionally, few to no sutures are used in the procedure and minimal astigmatism is introduced. With this method, less foreign antigen is introduced to the donor and the incidence of vascular ingrowth and graft rejection are lowered. A partial thickness corneal transplant provides for faster visual recovery and improved globe stability (Fernandez and Afshari 2010).

Indication

The cornea is composed of the following layers from anterior to posterior: epithelium, Bowman's membrane, stroma, Descemet's membrane, and endothelium. The cornea is maintained in a state of deturgescence by the Na^+/K^+ ATPase on the endothelial cells and the tight junctions between the cells that limit the movement of fluid into the stroma. By maintaining the cornea at an optimal level of hydration, the endothelial cells preserve the ordered arrangement of collagen, which is essential for corneal transparency. Once damaged or lost, endothelial cells cannot be physiologically replaced (Fernandez and Afshari 2010). Corneal endothelial dysfunction is the major indication for most of the penetrating keratoplasty (PKP) procedures that are performed in the United States annually. However, because endothelial dysfunctions often initially only affect certain layers of the cornea, corneal surgeons have moved toward selective endothelial keratoplasties for surgical replacement with donor tissue.

Deep lamellar endothelial keratoplasty is indicated for procedures that cause irreversible corneal endothelial dysfunctions, including the following:

1. Posterior corneal dystrophies, such as Fuch's dystrophy, nonguttate endothelial dystrophy, and posterior polymorphous dystrophy
2. Aphakic and pseudophakic corneal edema and bullous keratopathy
3. Iridocorneal endothelial syndrome (ICE)
4. Other causes of endothelial dysfunction, including trauma, foreign body, and age (Hannush 2011)

Descemet's stripping endothelial keratoplasty (DSEK) and Descemet's stripping automated endothelial keratoplasty (DSAEK) are modifications of Melles' PLK procedure, which quickly replaced DLEK and PLK given their simplified techniques and better visual outcomes. However, there continue to be indications for DLEK in patients at high risk for complications unique to DSEK and DSAEK, such as graft dislocation. In DLEK, the stromal bed of the recipient is roughened, which allows for better adherence (Shamie et al. 2009).

Prolonged intraocular air in the anterior chamber has been proposed as a method to stabilize the graft. DLEK would be the procedure of choice in any condition in which retention of the intraocular air bubble in the anterior chamber would not be possible. Such conditions would include a stable anterior chamber intraocular lens, aphakia, and irreparable iris defects, which allow for movement of the air bubble to the posterior pole (Shamie et al. 2009).

Contraindication

The following conditions are considered contraindications for the DLEK procedure:

1. Corneal ectasias
2. Stromal dystrophies
3. Any other cause of stromal scarring or opacification, including infection, interstitial keratitis, and lipid keratopathy
4. Anterior corneal dystrophies and degenerations, including Reis-Bücklers, Salzmann's, and Meesmann's (Hannush 2011)

Techniques and Principles

DLEK surgery is usually done under retrobulbar block anesthesia with a seventh cranial nerve block. This allows for both anesthesia and akinesia of the lids. General anesthesia may be used in patients who are uncooperative or in whom posterior pressure must be minimized. The DLEK procedure may be performed in combination with a cataract extraction. In such cases, cataract extraction is done prior to DLEK and after epithelial scraping to improve visualization if significant corneal haze is present. Dispersive viscoelastic agents should be avoided as they may adhere to the stromal interface and prevent adherence or the donor disk to the recipient stromal bed. The cataract surgery should be performed through a separate scleral limbal incision, which should be sutured tightly prior to creation of the stromal pocket of the DLEK procedure (Shamie et al. 2009).

Preparation of the Recipient Cornea

In DLEK, the corneal surface is left untouched in an effort to preserve the natural corneal topography, and the corneal limbus is preserved in order to maintain the globe's structural integrity (Terry 2003). The DLEK procedure is usually performed from the temporal side for ease of entry. A circular corneal marker, ranging in size from 8.0 to 9.0 mm, is used to create a circular imprint on the corneal surface. A sterile marker is then used to accentuate the circular indentation with dotted marks, which will serve as the template for the posterior lamellar resection that is done later in the procedure. Two 1.0 mm diameter corneal limbal stab incisions are placed 5 o'clock hours apart, which will be used as entry points to the anterior chamber. A 1.0 mm diamond knife is preferred as it creates a better paracentesis wound with easier anterior chamber entry compared to a metal blade. These entry ports can be marked with a sterile marker to allow for ease of identification and reentry. The cohesive viscoelastic Healon can be into the anterior chamber through one of the stab incisions, replacing the aqueous to maintain normal pressure during the procedure (Shamie et al. 2009).

A conjunctival peritomy is performed prior to creation of the 5.0 mm temporal scleral tunnel. Cautery is used for hemostasis. A 5.0 mm length incision with a depth of 350 μm is created 1.0 mm posterior and parallel to the superior corneal limbus temporally (Shamie et al. 2009). This incision is made using a trifaceted, guarded diamond knife. A specialized semisharp stromal dissector is then used to dissect a deep lamellar pocket at a depth of 80% into 1.0 mm of clear cornea. Straight and curved stromal dissectors are then used to extend the lamellar pocket beyond the pupillary axis. The lamellar pocket is extended from limbus to limbus (Terry 2003). This step is technically challenging, particularly locating the appropriate plane for dissection and preventing perforation of the cornea. Devers dissectors have sharp tips with blunt sides, which can be used to create this lamellar interface without perforating the cornea. After the stromal pocket has been created, additional Healon should be used to fill the chamber. A 2.8 mm keratome is then used to enter the anterior chamber through the scleral tunnel at the proximal mark of the corneal circular template mark (Shamie et al. 2009).

Microscissors are used to excise a posterior disk of the recipient's cornea using the circular template made on the surface of the cornea, and the wound is extended to measure 5.0 mm. The lamellar disk is removed using Utrata forceps. A 10–0 nylon, interrupted suture is placed in the corneal wound to maintain the anterior chamber while keeping a 3.0 mm opening. The cohesive viscoelastic Healon is then removed through this opening. The chamber is maintained with balanced saline solution (BSS) (Shamie et al. 2009).

Preparation of the Donor Cornea

Next, the donor cornea must be prepared for grafting. The donor tissue may be precut by an automated keratome, or the surgeon may prepare it. If the surgeon chooses to cut the donor tissue, an artificial anterior chamber with a microkeratome can be used to prepare the donor lamellar graft. The anterior chamber must initially be injected with Optisol-GS until a meniscus is formed on the post (Shamie et al. 2009). The corneal-scleral

cap tissue received from an eye bank is coated with Healon on the endothelial side and placed onto the post of the artificial anterior chamber with the endothelial side down (Terry 2003). Another less common practice is to place the donor cornea epithelial side down on the artificial anterior chamber to prevent endothelial cell compromise. The donor cornea is then capped into place and more Optisol-GS is injected into the artificial anterior chamber until the desired pressure is achieved. Then a sterile marker is used to mark the central cornea and the horizontal meridian peripherally (Shamie et al. 2009).

For manual lamellar dissection, random and scattered marks can be made on the corneal surface to help visualize the depth of dissection. A Barron suction recipient trephine with a diameter 0.5 mm larger than the desired donor graft size is placed over the donor tissue, suction is applied, and trephination is done to about 60% depth. The trephine should be removed and the cut should be inspected. The lamellar pocket dissection is then done at 80% depth through the donor tissue with the crescent blade and stromal dissectors. It can also be initiated with the trifaceted diamond knife set at 350 μm (Shamie et al. 2009).

When using an automated microkeratome, the artificial anterior chamber should be pressurized by injecting Optisol. A Barraquer tonometer should be used to verify that the pressure is at least 65 mmHg. The epithelium is then removed with a Merocel surgical sponge, and the microkeratome is set into its gear tract without the stopper. A Merocel sponge soaked in Optisol is used to pain the surface of the cornea, and the microkeratome cut is made smoothly across the cornea. The cut cap is examined for completion of the cut, thickness, and diameter. The diameter of the cut cap should be at least 1.0 mm larger than the planned graft to allow a 0.5 mm margin of error in centration. If the cap size is inadequate, the surgeon can manually extend the lamellar dissection. The outer edge of the exposed stromal bed is demarcated with small dots to allow for improved centration of the trephine in later steps of the procedure. Merocel sponges are used to dry the stromal bed and the free cap replaced in the proper orientation (Shamie et al. 2009).

When manual dissection of the donor graft is done, the dissection should extend to the metal cap of the artificial anterior chamber that ensures a large margin of error in case of accidental decentration. The pedestal of the artificial anterior chamber is slowly lowered. Optisol is injected into the anterior chamber during this step to prevent trauma to the endothelial cells. When adequate separation is established between the pedestal and the metal cap, the ends of the tissue are freed from the artificial anterior chamber's metal cap. This is done by gently nudging with the tip of closed forceps. The tissue is gently removed from the pedestal, allowing the cohesive Healon to fall away in one piece, and residual Healon may be washed away with Optisol (Shamie et al. 2009).

If precut tissue from the eye bank is used, the donor graft is placed with the endothelial side down onto a sterile, lint-free surface. The tissue is then placed endothelial side up onto a standard punch trephine block and a donor button of the same size is punched. A linear ribbon of Healon is injected into the horizontal meridian of the donor graft. The tissue is folded asymmetrically into a taco-like shape with the endothelial surface facing inward (Shamie et al. 2009).

Donor Graft Insertion and Attachment

All previously placed sutures placed in the 5.0 mm tunnel wound should be removed. The folded donor graft is held with specialized forceps and swiftly inserted into the anterior chamber. If the anterior chamber partially collapses as the forceps exit the wound, BSS should be injected through the paracentesis ports to deepen the chamber. The scleral wound may need to be closed with 10–0 nylon sutures to maintain the depth of the chamber. At this point, the donor tissue is already partially adherent to the recipient stromal bed and has begun to unfold perpendicular to the plane of the iris (Shamie et al. 2009). The tissue is thought to initially self-adhere because of the hydrophilic attraction between wet tissues. An

air bubble can be injected into the anterior chamber between the two sides of the donor tissue at this juncture to aid in its unfolding and reinforce adhesion of the donor tissue (Terry 2003).

A reverse Sinskey hook or an equivalent instrument may be necessary for final positioning of the donor disk. The hook is inserted into the anterior chamber from one of the side ports furthest from the direction in which the disk must be shifted, and the hook is used to gently push the graft into position. This is easier done when the anterior chamber is only partially filled with an air bubble. Once the graft is in place, the anterior chamber is completely filled with an air bubble, and any interface fluid is swept out. The wound is then fully closed, knots buried, and conjunctiva is closed. The air bubble is fully removed and replaced with BSS. When the air is replaced, the adherence between the tissues is thought to result from the donor endothelial pump function creating stromal suction adherence (Terry 2003).

Outcome

DLEK preserves the normal corneal surface, and thus it has many benefits over PKP. DLEK does not require penetrating corneal wounds and avoids the need for surface sutures. The lack of surface sutures in DLEK results in lower risk of suture-related complications, such as irregular refractive astigmatism, unpredictable corneal curvature, suture-related graft rejection, and infections. Additionally, because selective suture removal is not a component of the DLEK procedure, rigorous and prolonged follow-up is not required. Because the scleral tunnel wound of endothelial keratoplasty has greater tensile strength than the wound of PKP, DLEK results in more rapid wound healing (Shamie et al. 2009). The procedure also results in marked stability and preservation of the preoperative keratometry readings, making posttransplant corneal power predictability possible and allowing for the DLEK procedure to be combined with cataract extraction and IOL placement. Compared to PKP, the stromal wound of DLEK appears to be quite stable (Terry 2003). Studies of donor endothelial survival after DLEK have revealed cell loss that continues for several years after surgery and stabilizes at 60–72% cell loss by 5 years postoperatively (Terry 2011).

Complications

Despite its many benefits, the DLEK procedure is technically challenging, which limits its utility on a large scale. Additionally, the deep lamellar dissection in both the donor and recipient forms an interface between the deep stroma to stroma. It has been postulated that this interface limits the final visual potential postoperatively (Shamie et al. 2009). There is minimal risk of graft dislocation, which occurs at a rate of less than 3% (Terry 2011). Another potential complication of DLEK is the posterior migration of the air bubble injected into the anterior chamber, which can result in pupillary block or secondary angle closure glaucoma with increased postoperative intraocular pressures (Shamie et al. 2009).

Cross-References

- ▶ Corneal Dystrophy
- ▶ Iridocorneo Endothelial Syndrome

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Degeneratio Hyaloidea Grannuliformis Corneae

- ▶ Keratinoid (Spheroidal) Degeneration
- ▶ Keratopathy Actinic (Labrador Keratopathy/ Spheroidal Degeneration)
- ▶ Spheroidal Degeneration

Degenerative Myopia

- ▶ Pathologic Myopia

Degenerative Retinoschisis, Typical and Reticular

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Synonyms

Retinoschisis

Definition

Retinoschisis is characterized by the abnormal splitting of the ▶ retina's layers. Most frequently, it is observed at the inferotemporal peripheral fundus and is often a bilateral condition. Characteristically, it is a well-defined, circumscribed, smooth, dome-shaped elevation of the inner retina extending posteriorly from the ora serrata.

Etiology

Pathogenesis is unknown but chronic vitreous traction in the periphery of retinal areas predisposed to suffer degenerative changes may play a role.

Histologically, there is splitting of the retinal layers, which starts at the external plexiform layer (EPL). This causes cystoid cavities in the EPL that contain a viscous mucopolysaccharide-rich substance. A microscopic degeneration of neuroretinal and glial supporting elements is observed. This entity is known as typical peripheral cystoid degeneration, a condition that is present in almost all adults to some extent. Its coalescence and cavity extension causes typical retinoschisis. This is a slow, gradual process resulting in the complete destruction of the neurons in the area with absolute loss of vision in the corresponding zone.

Posterior and continuous to typical peripheral cystoid degeneration, another entity may appear. This is reticular peripheral cystoid degeneration, which is much less common. The cystoid spaces in this case are located in the nerve fiber layer. Progression of this condition may lead to reticular degenerative retinoschisis ("bullous" retinoschisis).

Retinoschisis Classification

1. **Degenerative**
   - Typical
   - Reticular
2. **Hereditary**
   - X-linked juvenile retinoschisis
3. **Tractional**
4. **Exudative**
   - Secondary to optic disc pit

Clinical Presentation

Most common forms are asymptomatic and non-progressive. In both degenerative forms, possible

symptoms presented include sporadic photopsia, floaters, visual acuity loss (depending on the affected area), and absolute scotoma of the visual field.

Diagnosis

Although described as two different entities, it is often difficult to differentiate clinically between typical and reticular retinoschisis.

Indirect ophthalmoscopy and biomicroscopy help to differentiate retinal detachment because of the individual characteristics. External scleral depression improves visualization when the retinoschisis is located at the periphery and does not extend far from the *ora serrata*. It also detects changes in the outer layers.

Typical Degenerative Retinoschisis

The splitting of the layers occurs at the external plexiform layer level. With ophthalmoscopy, an oval elevation most commonly located at the inferotemporal quadrant of the outer retina is observed. Irregular small white spots ("snowflakes") may be occasionally observed in the posterior zone of the degenerative area; but the origin of these spots is still unclear. It is believed that they may belong to Müller cell remains or to neurons that form bridges within the zone. Sclerotic retinal vessels are found within the zone, as well as cystoid degeneration anterior to schisis.

It is rare to find typical degeneration in the macular area or holes within the zone and therefore retinal detachment is uncommon.

Reticular Degenerative Retinoschisis

This is associated with more complications such as progression to the posterior pole and retinal detachment. In most cases, it appears at the inferotemporal quadrant and is associated with hypermetropia and bilateral affection in 50–80% of cases. There is approximately 23% incidence of holes in the external layer, therefore with a higher risk of retinal detachment. However, it is estimated that retinal detachment risk is around 0.04%.

Large posterior retinoschisis is more likely to develop outer wall holes that may cause shallow retinal detachment even in the absence of inner retinal holes. This shallow retinal detachment may difficult to diagnose before it extends beyond the posterior edge of the retinoschisis.

Other auxiliary tests:

Wide-field retinography: for follow-up, in order to evaluate progressions or new associated lesions.

Visual fields: absolute scotomas are found at the area affected by retinoschisis.

Spectral domain optical coherence tomography (*SD-OCT*): for the visualization and identification of the separated layers.

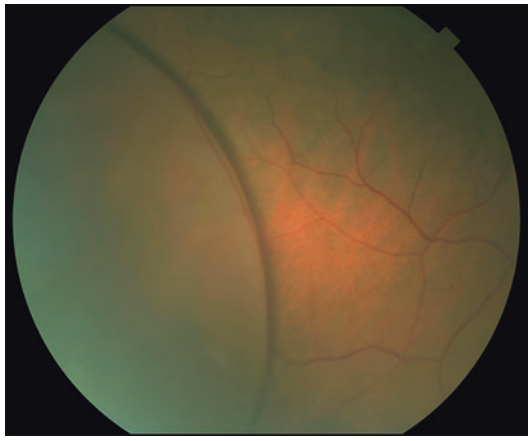
Fluorescein angiography: shows no changes at the underlying retinal pigment epithelium (RPE) unless there are holes or retinal detachment. In some cases, retinal leakage into the inner layers may be observed.

Lab Diagnostics

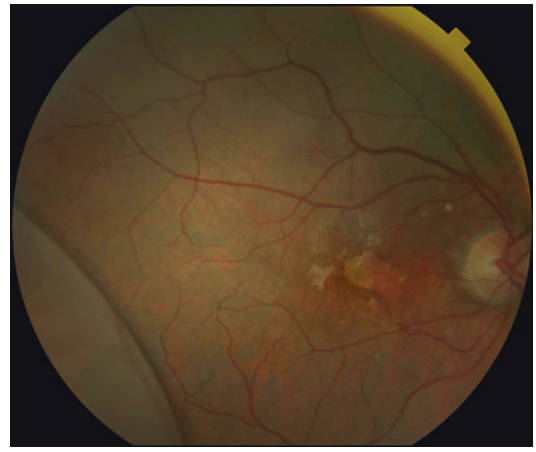
No need for typical or reticular retinoschisis. Only in the rare event of needing to confirm the diagnosis of X-linked juvenile retinoschisis, a genetic DNA may be performed. Systemic studies are not necessary.

Differential Diagnosis

This must be performed in the case of rhegmatogenous retinal detachment. Features may sometimes be similar, especially in chronic retinal detachment. Retinoschisis generates an absolute scotoma in the affected area, whereas rhegmatogenous retinal detachment causes relative scotoma.



Degenerative Retinoschisis, Typical and Reticular, Fig. 1 Large posterior retinoschisis extending to the posterior pole of the right eye in a 85 years-old male. The patient has been followed-up closely due to frequent visits to treat exudative AMD in the same eye. The retinoschisis has not shown further posterior progression for the last 3 years and has not shown outer layer holes. No treatment for the retinoschisis has been required



Degenerative Retinoschisis, Typical and Reticular, Fig. 2 Large posterior retinoschisis extending to the posterior pole of the right eye in a 85 years-old male. The patient has been followed-up closely due to frequent visits to treat exudative AMD in the same eye. The retinoschisis has not shown further posterior progression for the last 3 years and has not shown outer layer holes. No treatment for the retinoschisis has been required

Signs such as tobacco dust and vitreous hemorrhage found frequently in retinal detachment are not present in retinoschisis.

In retinoschisis, the separated surface appears smooth and regular, whereas in retinal detachment, it is irregular and corrugated, not dome shaped. However, old chronic rhegmatogenous retinal detachment may look like retinoschisis due to the thin, smooth detached retina. Long-standing retinal detachments will usually show demarcation lines and atrophy of underlying RPE, which will help to differentiate this from retinoschisis.

There are no specific changes at the foveal area, unlike in patients with X-linked juvenile retinoschisis.

SD-OCT may be useful in differential diagnosis in certain cases when the macula is affected in order to rule out vitreomacular traction or schisis secondary to optic disc pit.

Therapy

Retinoschisis anterior to the equator is followed up. Larger retinoschisis posterior to the equator may be observed in the absence of outer retinal holes. In large posterior retinoschisis that shows progression toward the posterior pole or has outer retinal holes, a prompt photocoagulation treatment is required in order to avoid complications. Laser is applied at the posterior edge of the retinoschisis, around the outer retinal holes or both, in cases of progression and presence of outer retinal holes (Figs. 1 and 2).

When shallow retinal detachment is present, laser therapy may still be effective in some cases, around the outer holes and as a barrier posterior to the retinoschisis.

If retinal detachment is larger, surgical repair with vitrectomy and intravitreal gas is required.

Prognosis

For typical degenerative retinoschisis anterior to the equator or minimally posterior to it, and with the absence of outer retinal holes, the prognosis is favorable and monitoring may be annual. Other situations, as described previously, will be followed up carefully and proactively treated in order to prevent retinal detachment or progression of the retinoschisis into the macular area.

Epidemiology

Related to aging, according to some case series, incidence varies from 4% to 20% in persons of 40 years or older.

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Delayed Acute Photophobia

► Transient Light-Sensitivity Syndrome

Deliberate Disability

► Munchausen Syndrome

Delle (Singular)

► Dellen

Dellen

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Synonyms

Delle (singular)

Definition

First described in 1911, dellen are saucer-like depressions in the corneal surface, typically at the corneal margin, caused by interruptions of the tear film and resultant local dessication of the cornea. Surface elevations such as those produced by dermoids, pterygia, large filtration blebs, significant chemosis, or tissue interruption from a limbal approach to muscle surgery prevent the eyelid from adequately resurfacing the cornea with tear fluid during blinking. Local stromal dehydration and thinning are accompanied by punctate irregularities of the epithelium, mild discomfort, or rarely pain. Treatment with frequent ocular lubrication, with or without a bandage contact lens, restores stromal hydration and provides symptomatic relief. Surgical management (e.g., bleb revision) is reserved for severe cases that are unresponsive to medical therapy. Though rare, untreated dellen can cause descemetocele formation or lead to corneal perforation.

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Demyelinating Disease

► Diplopia in Multiple Sclerosis

Demyelinating Optic Neuropathy

► Optic Neuritis: Overview

Demyelination, in Multiple Sclerosis, Optic Neuritis

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Definition

Demyelination is the hallmark pathologic finding in the disease multiple sclerosis (MS).

Etiology

Although there are several theories regarding the etiology of demyelination in MS, the most widely accepted view is that immune dysregulation leads to demyelination of the central nervous system (CNS). Early on in the disease, oligodendrocytes are shown to help regenerate myelin after attacks from T cells (although some studies implicate B cells and natural killer (NK) cells); however, as the disease progresses, the destructive processes of the immune system overtake the rate of regeneration leading to a neurodegenerative condition. Despite these theories, autopsies have demonstrated that the actual cause of tissue damage is variable. Relatives of patients with MS have a higher risk of developing the disease; however the genetic contributions to this disease are likely multifactorial. Some studies have implicated genes coding for class two major histocompatibility complexes (MHC II), while other studies have implicated non-MHC genes such as genes regulating neurotrophic factors or chemokine receptors (Cohen and Rae-Grant 2010).

Clinical Presentation

The demyelination of various neurological pathways can lead to a wide range of clinical presentations including but not limited to visual problems, gait/motor problems, urinary symptoms, sexual dysfunction, cognitive impairment, and fatigue. 70 to 80% of patients begin with a relapsing-remitting course where new or worsening neurologic symptoms develop over days to weeks and then abate over the course of several weeks resulting in full or partial recovery. After 10–15 years, the accumulation of small deficits from each attack causes increased debilitation, and patients transition to secondary progressive MS. Unfortunately some patients begin with the progressive phase of the illness which is termed primary progressive MS (Cohen and Rae-Grant 2010).

Diagnostics

The most important tools for diagnosis of demyelination in MS are the history, physical, and magnetic resonance imaging (MRI) of the brain. The MRI is able to detect demyelination of current MS lesions, past MS lesions, and MS lesions that are currently asymptomatic. Combined with the history and physical, one can identify MS due to its dissemination over both anatomical space and time. Other diagnostic tools include cerebrospinal fluid (CSF) analysis and evoked potentials. CSF analysis can show increased IgG antibodies and/or myelin basic protein, whereas evoked potentials will demonstrate slowed conduction velocity of brain stem pathways. However, these tests are typically only used as confirmation (Cohen and Rae-Grant 2010).

Differential Diagnosis

The demyelination in MS has a presentation similar to that of other central nervous system (CNS) insults such as monophasic CNS inflammatory demyelinating syndromes, fulminant idiopathic CNS inflammatory syndromes, inflammatory/immune syndromes, infection, vascular complications, genetic/degenerative diseases, metabolic disorders, neoplasms, and spinal disorders (Cohen and Rae-Grant 2010).

Therapy

The mainstay treatment for MS attacks is corticosteroids. They help with the recovery and theoretically might help to delay the next relapse; however, the prophylactic efficacy of this treatment is not strongly supported by research. All other treatments are considered disease-modifying agents since their goal is not to cure MS or reverse any of the damage caused by demyelination but rather to prevent further relapses. One such agent, glatiramer acetate, is a mixture of peptides that is theorized to bind MHC II sites on T cells, inhibiting their inflammatory actions. Interferon beta is another common treatment that modulates B- and T-cell functioning, helping to regenerate the blood-brain barrier and reduce cytokines. The humanized monoclonal antibody natalizumab prevents migration of leukocytes into the CNS by binding and inhibiting integrin. In addition, mitoxantrone can be used as a chemotherapeutic agent to suppress the immune system. The overall goal of these treatments is to suppress the immune system in order to prevent demyelination (Cohen and Rae-Grant 2010).

Prognosis

Prognosis is uncertain given that this disease has a variable presentation. Roughly 5% of patients have a rapidly progressing disease that can lead to early debilitation and mortality; however, another 10–20% have a relatively benign form of the disease that will lead to minimal debilitation. Some factors such as female sex, predominantly sensory symptoms, and few MRI lesions suggest a more favorable prognosis, while the male sex; pyramidal, cerebellar, or cognitive symptoms; and many MRI lesions indicated a less favorable prognosis. Nevertheless, patients with presumed good prognostic factors can have a rapidly progressing disease, while patients with poor prognostic factors can have a more indolent disease (Cohen and Rae-Grant 2010).

Epidemiology

MS affects roughly 400,000 people in the US and 200,000 people around the world with a prevalence of about 1/1,000 worldwide. The onset of the disease typically begins between the second and fourth decade of life with women being affected more than men in a 3:2 ratio. In addition, the disease occurs more in patients living at higher latitudes in both the northern and southern hemispheres. There have been no environmental factors implicated in MS, but there is likely a combination of environmental and genetic factors that predispose one to developing this disease (Cohen and Rae-Grant 2010).

Cross-References

- ▶ Optic Neuritis
- ▶ Poser Criteria, for Multiple Sclerosis
- ▶ WEBINO ("Wall-Eyed" Bilateral Internuclear Ophthalmoplegia) Syndrome

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Deoxycholate Amphotericin (D-AmB)

- ▶ Amphotericin B, for *Aspergillus* Endophthalmitis

Dermabond

► Cyanoacrylate Adhesive

Dermatitis

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Synonyms

Atopic dermatitis; Contact dermatitis; Eczema

Definition

Dermatitis generally refers to pruritic, erythematous, and inflamed skin that is most commonly caused by allergens or irritants. Ocular complications include eyelid dermatitis, chronic blepharitis, keratoconjunctivitis, vernal conjunctivitis (with cobblestoning of the palpebral mucosa), keratoconus, uveitis, retinal detachment, and cataracts. Chronic scratching of the eyelid may lead to corneal abrasion. Dennie-Morgan lines are single or double folds beneath the lower eyelids that are diagnostic for atopic dermatitis.

Cross-References

► Blepharitis
► Cataract, Causes and Treatment
► Edema, Eyelid
► Eyelid Erythema
► Keratoconjunctivitis: Overview
► Keratoconus
► Other Uveitic Etiologies
► Retinal Detachment
► Vernal Conjunctivitis

Dermis-Fat Grafts

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Definition

A graft that provides volume augmentation, eliminates the risk of implant extrusion, and preserves the conjunctiva, advancing it in the fornices, thereby providing deeper forniceal spaces.

Indications

There are several indications for using a dermis-fat graft (DFG). The most common are as follows:

1. Extrusion or migration of orbital implant following enucleation
2. Expand or augment orbital volume
3. Treatment of contracted sockets in order to preserve conjunctiva and advance it in the fornices
4. Augment superior sulcus deformities
5. Primary implant after enucleation or evisceration (2008)

Techniques and Principles

DFG is usually performed under general anesthesia, and the donor site of the graft may be the lower abdomen, thigh, or inferomedial buttocks, depending on the surgeon's preference. Local anesthesia is given to the orbit and the donor site.

In cases of an extruding implant or one which has severe contractures, the conjunctiva is incised and the implant, if present, is removed. Muscle

remnants within the socket should be identified if possible. This allows for greater graft survival (due to the vacularity the muscles provide to the graft) and motility of the socket. An approximate 20–25 mm diameter DFG is harvested from the donor site first by removing the epithelium. A sharp blade is then used to incise subcutaneous tissue and fat to a depth of 15–20 mm in a circular fashion. The graft is then sutured into the socket onto a vascularized source (i.e., extraocular muscles or orbital fat). The dermis is left bare to epithelialize from the surrounding conjunctiva. A temporary conformer is placed. Full epithelialization of the dermis occurs in approximately one month. An ocular prosthesis can be fitted in 2–3 months (Stewart 1995).

Outcomes

Allows for enhanced orbital volume or increased socket surface area in cases of contractures or wound dehiscences.

Complications

Complications can occur intraoperatively and postoperatively. Intraoperative complications include removal of the wrong eye and orbital hemorrhage. Postoperatively, hemorrhage, edema, infection, delayed would healing, central graft necrosis and ulceration, central pitting, and graft failure can complicate the course of recovery. Fat atrophy and resulting loss of volume are variable; the rates increase in cases of compromised orbital vascular supply or the inability to isolate and attach the extraocular muscles to the dermis.

Cross-References

- ▶ Anophthalmic Socket
- ▶ Contracted Socket
- ▶ Enucleation
- ▶ Evisceration
- ▶ Ocular Prostheses

References

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Stewart WB (1995) Surgery of the eyelid, orbit, and lacrimal system, vol 3. AAO, San Francisco, pp 84–111

Descemet's Deep Anterior Lamellar Keratoplasty

▶ Deep Anterior Lamellar Keratoplasty (DALK)

Descemet's Membrane Endothelial Keratoplasty (DMEK)

▶ Lamellar Keratoplasty

Descemet's Stripping Endothelial Keratoplasty (DSEK)

▶ Lamellar Keratoplasty

Descemetocele

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Synonyms

Impending perforation

Definition

Descmetocele refers to focal, near-complete thinning of the cornea, with total destruction

of the epithelium and stroma in an area where Descemet membrane and corneal endothelium remain and bulge anteriorly. It is dome-shaped and translucent in appearance, often in contrast to a surrounding melting or necrotic process. If leaking, the lesion has progressed by definition to perforation. Presence of Descemetocele often portends a poor prognosis (Honig and Rapuano 2004).

Cross-References

► Corneal Ulcers

References

Honig MA, Rapuano CJ (2004) Management of corneal perforations. In: Krachmer JH, Mannis MJ, Holland EJ (eds) Cornea, 2nd edn. Mosby, Maryland Heights, 1670

Desferal

► Desferrioxamine Retinopathy

Desferoxamine B

► Desferrioxamine Retinopathy

Desferrioxamine B

► Desferrioxamine Retinopathy

Desferrioxamine Mesylate

► Desferrioxamine Retinopathy

Desferrioxamine Retinopathy

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Synonyms

Desferrioxamine mesylate; Desferal; Desferoxamine B; Desferrioxamine B; DFB; DFOA; DFO-B; Induced retinal toxicity; Retinopathy

Definition

Desferrioxamine is a bacterial siderophore produced by the Actinobacteria *Streptomyces pilosus*. Its main medical use is as a chelating agent, used to remove excess iron from the body. The mesylate salt of desferrioxamine is commercially available.

Desferrioxamine mesylate is frequently used to treat hemochromatosis, a chronic disease of iron accumulation, that can be either genetic or acquired. Acquired hemochromatosis is common in patients with certain types of chronic anemia (e.g., thalassemia and myelodysplastic syndrome), who require regular blood transfusions, which can greatly increase the amount of iron in the body. Desferrioxamine has also been used for the treatment of acute iron intoxication, especially in small children, and as a screening test for increased aluminum body stores in chronic renal failure. It can be used to treat aluminum toxicity in selected patients and to minimize doxorubicin cardiotoxic side effects.

Desferrioxamine has a high affinity for ferric iron (Ka 1031), and it removes iron from hemosiderin and ferritin, and, to a lesser extent, transferrin. It is most commonly administered as a slow subcutaneous infusion (over a period of 8–12 h each day), but can also be given intramuscularly or, less commonly, intravenously.

Adverse reactions of desferrioxamine have been reported for most major organ systems,

including cutaneous, cardiovascular, respiratory, gastrointestinal, and nervous systems. Severe side effects of desferrioxamine include bone dysplasia and auditory toxicity, consisting of high-frequency sensorineural hearing loss. Ocular findings of desferrioxamine toxicity include cataract, optic neuropathy, and pigmentary retinopathy involving the macula, as well as in some cases, the midperiphery or entire retina.

Desferrioxamine ocular toxicity first came to light in 1983 (Davies), when four patients with 13-thalassemia major were treated with a high intravenous dose to counter the effects of transfusion-induced iron overload. Two of them developed night blindness and visual field defects, which were improved on withdrawal of the drug.

Since then, numerous cases of desferrioxamine retinopathy have been described; however, the literature contains conflicting reports regarding the incidence, severity, and reversibility of desferrioxamine retinopathy, as well as the toxic desferrioxamine dosage or safe administration protocol. A retrospective study carried in a large pediatric center concluded that desferrioxamine-related ocular toxicity is a rare and mild finding; of a total of 84 children that received regular desferrioxamine treatment for transfusional hemochromatosis, related ocular toxicity was found only in one patient (1.2%).

Symptoms of desferrioxamine toxicity include decrease in central vision, metamorphopsias, difficulty in night vision, visual field defects, and photopsias. Characteristic fundus lesions of desferrioxamine retinopathy include pigmentary degeneration in the macula, peripapillary region, and periphery, retinal pigment epithelium (RPE) atrophy, pattern dystrophy – like maculopathies and bull's-eye maculopathy. Other ocular findings include cataract (sunflower shaped), optic disc edema, and optic atrophy.

Phenotypic investigation of desferrioxamine retinopathy has been based on ophthalmoscopy and fundus photography used for screening asymptomatic patients. Until recently, fluorescein angiography (FA) was used for detection and monitoring of presumed retinal toxicity. In the early FA stages, there is patchy blocked fluorescence or mottled fluorescence, followed in most patients by late hyperfluorescence. Optic disc hyperfluorescence is evident in some patients as well. However, fundus autofluorescence (FAF) imaging is probably superior to ophthalmoscopy in detection of early characteristic RPE abnormalities in patients at risk of desferrioxamine retinopathy, as well as in monitoring the disease progression over time. Abnormal FAF was classified into four phenotypic patterns: minimal change, focal, patchy, and speckled.

Recently, Viola et al. retrospectively reviewed charts and multimodal imaging of 20 patients with b-thalassemia diagnosed with desferrioxamine retinopathy after a minimum of 10 years of DFO treatment. Mean age was 45 years, and mean duration of subcutaneous DFO therapy was 32 years (range, 20–52 years). Ten patients (50%) showed different types of pattern dystrophy-like fundus changes, including butterfly-shaped-like, fundus flavimaculatus-like, and fundus pulverulentus-like, and vitelliform-like changes. Ten patients (50%) presented only minimal changes in the macula; these patients were significantly younger than patients presenting other patterns ($P = 0.023$). Abnormal fundus autofluorescence and/or near-infrared reflectance signals corresponded to the accumulation of material located within the outer retina or in the Bruch's membrane – retinal pigment epithelium (RPE) complex on spectral domain optical coherence tomography. Follow-up examinations during a 40-month period revealed progressive development of RPE atrophy in areas of pattern dystrophy-like changes.

Electroretinogram (ERGs) and electrooculogram (EOGs) performed in symptomatic patients with desferrioxamine toxicity were mostly, with few exceptions, abnormal. ERG findings include prolonged rod and cone implicit times and reduced scotopic and photopic a and b wave amplitudes. EOG findings include reduced Arden ratio (light peak to dark trough) and no detectable EOG response. In addition to ERG and EOG, visual field, visual-evoked potential, and pattern electroretinogram testing may also be informative.

The precise pathophysiological mechanism of desferrioxamine retinopathy is still unknown; however, it is likely to be multifactorial. Animal experiments and histology studies in human eyes with desferrioxamine retinopathy have shown that the degenerative process affects primarily the RPE and Bruch's membrane. Rahi et al. documented light and electron microscopy changes in the retinal pigment epithelium (RPE) following treatment with high-dose desferrioxamine for systemic iron overload. The changes included loss of microvilli from the apical surface, patchy depigmentation, vacuolation of the cytoplasm, swelling and calcification of mitochondria, and disorganization of the plasma membrane. In addition, Bruch's membrane overlying degenerate RPE cells appeared abnormally thickened owing to the accumulation of large amounts of mature elastic fibers, pre-elastic oxytalan, and long-spacing collagen. However, whether these RPE changes were in part due to ocular siderosis is difficult to determine.

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Desquamating Skin Conditions

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Synonyms

Skin peeling conditions

Definition

Desquamating skin conditions are disorders in which the skin sheds in sheets or scales. Normally, terminally differentiated keratinocytes are shed as individual cells, but under pathological conditions, such as diseases like Stevens-Johnson syndrome or injury to the skin, keratinocytes are shed in clusters forming visible sheets or scales.

Cross-References

▶ Blepharitis
▶ Keratinocytes: Overview
▶ Stevens Johnson Syndrome

Detachment of the Retina Pigment Epithelium

▶ Pigment Epithelium Detachment

Developmental Glaucoma

▶ Primary Congenital Glaucoma

Dexamethasone Implant

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Introduction

In the past decade, the diseases of the posterior segment of the eye have constituted an area of unmet medical need and as a result became an important therapeutic target. Among the diseases of the posterior segment are the retinal vascular diseases, particularly diabetic retinopathy as well as retinal venous occlusive disease, as well as age-related macular degeneration and uveitis.

Historically, the most common drug delivery method for treating ocular disorders has been topical application, as it is more convenient and safe compared to systemic administration. To treat the above mentioned diseases, intraocular injections are now routinely applied in clinical practice. In order to minimize the number of injections, the therapeutic drug concentration should ideally be maintained for longer time periods. One way of achieving this is to load drugs onto polymeric implants releasing the active in a sustained manner, by diffusion or degradation of the polymer block (Eljarrat-Bienstock et al. 2010).

Pathology and Pathophysiology of Ocular Inflammation and Edema

Inflammatory components within the vascular tissue play a central role in the development of uveitis as well as in macular edema secondary to retinal vein occlusions and diabetic retinopathy. Inflammation is a protective tissue response to injury or destruction of tissues, which serves to destroy, dilute, or wall off both the injurious agent as well as the injured tissues (Kumar and Clark 2009).

Classic generalized systemic signs of acute inflammation are pain, heat, swelling, and loss of function (Marieb and Hoehn 2007).

In the retina there is no pain or redness, however swelling (edema), a variable loss of visual function as well as presence of cells and proteins (Augustin 2010).

Cell monolayer integrity or the vascular barrier can be disrupted by a number of different inflammatory agents. Angiotensin II, VEGF, prostaglandins, cytokines, interleukins, VCAM-1 and ICAM-1, as well as macrophages and neutrophils are part of the local inflammatory process. To date the complex chain of interaction of all these substances is not fully clarified (Pasqualetti et al.2007).

Edema and leakage due to inflammation are biochemically distinct from that induced by VEGF. Vascular permeability and the resulting macular edema is driven by both VEGF-independent and VEGF-dependant inflammatory pathways (Saishin et al. 2003).

In the development of macular edema, early stages of vasculature dysfunction are characterized by a breakdown of the blood retinal barrier, leading to accumulation of fluid and serum macromolecules in the intercellular space and in turn to loss of visual acuity (Girach and Lund-Andersen 2007; Kanski 2008).

In contrast, uveitis is primarily characterized by an inflammation of the uvea (iris, ciliary body, and choroidea), which may also lead to the development of macular edema (Kanski 2008).

Steroids for Intravitreal Use: Comparative Potencies, Mechanism of Action, Efficacy, and Safety

While the most commonly used steroids are dexamethasone, triamcinolone acetonide, and fluocinolone acetonide and all are structurally similar, they can be significantly differentiated by their aqueous and lipid solubility, delivery system requirements, pharmacokinetics, and interactions with functional glucocorticoid receptor (Edelman 2010).

Dexamethasone has the highest relative strength of any steroid used in ophthalmic practice. A single dose of 0.18 mg/ml dexamethasone is equivalent to 1 mg/ml triamcinolone acetonide in terms of corticosteroid efficacy (Kiernan and Mieler 2009).

The mechanism of action is thought to be complex. Corticosteroids act as anti-inflammatory, immunosuppressive, and antimitogenic agents (blocking the arachidonic acid pathway, formation of Il-1). They also have antiapoptotic (protection of signals evoked by cytokines, cAMP, tumor suppressors, and death cells), antiedematous (suppression of leukocyte adhesion to vessel walls), and antiangiogenic effects such as suppression of VEGF gene and the metabolic pathway of VEGF (Golan and Loewenstein 2010).

Data on their use in diseases of the posterior segment of the eye has been limited.

Initially only intravitreally applied triamcinolone acetonide was investigated, mostly in uncontrolled pilot trials and case studies. Only recently a variety of prospective randomized clinical trials as well as data analyses have shown a useful role of these compounds in the treatment of diabetic macular edema and macular edema secondary to retinal vein occlusion (Kiernan and Mieler 2009).

In uveitis, corticosteroid treatment remains the mainstay of management. While topical corticosteroids are effective to control anterior uveitis, systemic application is widely used for management of posterior forms, especially when both eyes are involved. However, in case of unilateral posterior inflammation, local therapy has shown to have considerable advantages. In such mild to moderate ocular uveitis cases, intraocular injections have recently proven to be a useful alternative to systemic medication (Taylor and Hazlita 2010).

Potential complications of intravitreal steroid treatment may be divided into steroid-related and injection-related adverse effects.

Intravitreal steroid treatment commonly causes formation or progression of cataract. In an elderly population, intravitreal triamcinolone treatment led to clinically significant cataract with eventual cataract surgery within 1 year after first injection. The steroid-induced rise of IOP is usually temporary and can normally be controlled with topical IOP-lowering medications in most cases. Only 1% of cases would require surgical intervention (Golan and Loewenstein 2010).

Injection-related side effects may include retinal detachment, vitreous hemorrhage, bacterial or noninfectious endophthalmitis, as well as pseudoendophthalmitis. Data have shown that less than 1% of cases would experience injection-related side effects.

Advanced Intravitreal Drug Delivery Systems: Concepts, Biodegradable and Non- Biodegradable Implants

The delivery of drugs to the posterior eye segment is difficult due to the long diffusion distance, the lens iris barrier, and the acellular nature of the vitreous body. Pharmacokinetics of drug diffusion is influenced by the sclera surface area and its thickness. Advanced delivery systems for posterior segment disorders can be divided into two categories. The first category includes gels, emulsions, viscosity enhancers, penetration enhancers, prodrugs, liposomes, and iontophoresis. The second category consists of nanoparticles, polymeric inserts, and implants (Eljarrat-Bienstock et al. 2010).

A number of nonbiodegradable and biodegradable implants have undergone clinical development to achieve sustained levels of steroids in the vitreous. Nonbiodegradable implants are usually reservoir implants suitable for long-term drug exposures. While the drug is released over the time the reservoir remains at the site of action and would need to be surgically removed.

Biodegradable implants are based on a polymer matrix system, where the active is distributed throughout the matrix and released as the polymer degrades. Degradation may occur by hydrolysis, leading to bulk erosion.

Biodegradable implants are typically constructed from synthetic aliphatic polyesters of the poly-α-hydroxy acid family, which include polyglycolic acid (PGA), polylactic acid (PLA),

and the PGA/PLA copolymer, polylactic-co-glycolic acid (PGLA). The ratio of lactic to glycolide used for the polymerization can be varied and will influence the biodegradation characteristics of the product. PGLA is easy to construct into various shapes such as rods, screws, plates and pins, suture material, as well as vascular grafts and stents. It is widely used in orthopedic and dental surgery. Biocompatibility of PGLA-containing sutures and fracture fixation devices has been confirmed in human clinical trials. PLA and PGLA biocompatibility has also been studied in ocular tissues, and the polymers have been suggested to show an even better tolerability than when placed in nonocular tissues.

These new delivery systems target a variety of retinal diseases, among them uveitis, DME, and ME secondary to RVO. They are meant to maximize efficacy in chronic diseases requiring frequent and repeated administration to the back of the eye over longer time periods. They are capable of a more controlled drug release, keeping a stable and sustained concentration of the drug at site of action and thus minimizing systemic exposure. Additionally, they are striving to improve safety by reducing the risk of complications due to the actual injection, such as injury to the lens, retinal detachment, and – most significantly – endophthalmitis. In cases where implants require one or more surgical procedures for placement or removal, however, patients are potentially at risk to experience associated complications (Kearns and Williams 2009; Kiernan and Mieler 2009; Lee et al. 2010).

Dexamethasone Implant

A Pharmacodynamic and Pharmacokinetic Properties

Within the WHO Anatomical Therapeutical Chemical (ATC) classification system, the Dexamethasone Implant is grouped as an ophthalmological and anti-inflammatory agent (ATC code: S01BA01). Dexamethasone, a potent corticosteroid, has been shown to suppress inflammation by inhibiting edema, fibrin deposition, capillary leakage, and phagocytic migration of the inflammatory response. Vascular Endothelial Growth Factor (VEGF) is a cytokine which is expressed at increased concentrations in the setting of macular edema. It is a potent promoter of vascular permeability. Corticosteroids have been shown to inhibit the expression of VEGF. Additionally, corticosteroids prevent the release of prostaglandins, some of which have been identified as mediators of cystoid macular edema.

The Dexamethasone Implant consists of a polylactic-co-glycolic (PGLA) rod-shaped matrix (Novadur ^{TM}) loaded with 700 μg dexamethasone.

Plasma concentrations were obtained from a subset of 21 patients in two, 6-month efficacy studies prior to dosing and on day 7, 30, 60, and 90 following the intravitreal implant containing 350 μg or 700 μg dexamethasone. Ninety-five percent of the plasma dexamethasone concentration values for the 350 μg dose group and 86% for the 700 μg dose group were below the lower limit of quantitation (0.05 ng/ml). The highest plasma concentration value of 0.094 ng/ml was observed in one subject from the 700 μg group. Plasma dexamethasone concentration did not appear to be related to age, body weight, or sex of patients.

In a 6-month monkey study following a single intravitreal injection of Dexamethasone Implant, the dexamethasone vitreous humour C_{max} was 100 ng/ml at day 42 postinjection and 5.57 ng/ml at day 91. Dexamethasone remained detectable in the vitreous at 6 months post-injection. The rank order of dexamethasone concentration was retina > iris > ciliary body > vitreous humour > aqueous humour > plasma.

In an in vitro metabolism study, following the incubation of [14C]-dexamethasone with human cornea, iris-ciliary body, choroid, retina, vitreous humour, and sclera tissues for 18 h, no metabolites were observed. This is consistent with results from rabbit and monkey ocular metabolism studies.

Dexamethasone is ultimately metabolized to lipid and water soluble metabolites that can be excreted in bile and urine (Ozurdex Summary of Product Characteristics 2013).

The Dexamethasone Implant polylactic-co-glycolic (PGLA) matrix represents a bulk eroding polymer. The biodegradation rate of PGLA is governed by the proportion of lactide and glycolide, i.e., the higher the glycolide content, the faster the degradation rate. The PGLA matrix exhibits a biphasic release of the drug: an initial diffusion of the drug at or near the surface of the matrix with a higher dose over a period of 6 weeks is followed by a lag phase releasing lower but therapeutic doses for up to 6 months. This happens by the polymer achieving bulk erosion, resulting in a significant increase in pores or water channels, thus allowing the remaining drug to diffuse out of the porous implant structure. The initial dose is controlled by the total surface area of the implant, the dexamethasone loading, and its hydrophobicity. The second phase is well regulated by the speed of polymer degradation from the outside and inside. The matrix hydrolyses to lactic and glycolic acids; the lactic acid is further metabolized to H_2O and CO_2.

The Dexamethasone Implant is inserted through a single-use proprietary DDS intravitreal applicator system, using a 22 gauge biplanar injection. The small puncture caused is self-sealing (Kuppermann and Loewenstein 2010).

Clinical Data

Phase II clinical trial results with the Dexamethasone Implant demonstrated statistically significant therapeutic results. The study evaluated 306 patients who were diagnosed with macular edema due to four complicating conditions, among them uveitis, retinal vein occlusions, and diabetes. Participants were randomized to one of the following treatment groups: Dexamethasone 350 μg Implant, Dexamethasone 700 μg Implant, or control group. The trial showed that after 180 days, 21% of patients in the control group, 24.3% of patients receiving the lower concentration, and 32.4% of patients receiving the higher concentration achieved an improvement of at least two lines in their visual acuity ($p = 0.06$). There was also a significant decrease in retinal thickness and FA leakage in both dosing groups at 3 and 6 months. Three months after implantation contrast sensitivity was significantly better in the Dexamethasone 700 μg Implant group versus control. The trial reported relatively few adverse effects, except for mild cases of increased IOP. At the primary endpoint at 90 days 2% of patients treated with either Dexamethasone Implant showed an increase over baseline of $\geq$10 mmHg, compared to 1% in the observation group. All were successfully managed with either observation or IOP-lowering medication. Cataracts were present in 15% of the Dexamethasone 350 μg Implant group, 17.8% of the Dexamethasone 700 μg Implant, and 12.4% of the control group (Kuno and Fujii 2010); Kiernan and Mieler 2009; Kuppermann and Loewenstein 2010).

Efficacy and Safety in Central Retinal Vein Occlusion (CRVO) or Branch Retinal Vein Occlusion (BRVO)

Based on the results above two multicenter, double-masked, randomized, sham-controlled, parallel phase 3 studies of identical design were undertaken. Together they comprised 1,267 patients suffering from macular edema following central or branch retinal vein occlusion (CRVO/BRVO) who were randomized to receive treatment with dexamethasone 350 μg or 700 μg implants or control (sham injections). A total of 427 were randomized to the Dexamethasone 700 μg Implant, 414 to Dexamethasone 350 μg Implant, and 426 patients to control.

Based on the pooled analysis results, treatment with Dexamethasone Implants showed statistically significantly greater incidence of responders, defined as patients achieving a $\geq$ 15 letter improvement from baseline in best corrected visual acuity (BCVA) at 90 days following injection of a single implant, when compared with control ($p < 0.001$).

A treatment effect was seen at the first observation time point of day 30. The maximum treatment effect was observed at day 60, and the difference in the incidence of responders was statistically significant favoring the Dexamethasone

700 μg Implant compared with control at all time points to day 90 following injection. There continued to be a numerically greater proportion of responders for a ≥15 letters improvement from baseline in BCVA in patients treated with Dexamethasone 700 μg Implant compared with control at day 180.

The mean change from baseline BCVA was significantly greater with Dexamethasone 700 μg Implant compared to control at all time points.

In each Phase III study and the pooled analysis, the time to achieve ≥15 letters (3-line) improvement in BCVA cumulative response curves was significantly different ($p < 0.001$), with Dexamethasone Implant treated patients achieving a 3-line improvement in BCVA earlier than control treated patients. Dexamethasone Implant was numerically superior to control in preventing vision loss as shown by a lower of proportion of patients experiencing deterioration of vision of ≥15 letters in the Dexamethasone Implant group throughout the 6-month assessment period. In each of the phase III studies and the pooled analysis, mean retinal thickness was significantly less, and the mean reduction from baseline was significantly greater, with Dexamethasone Implant (−207.9 μm) compared to control (−95.0 μm) at day 90 ($p < 0.001$, pooled data). The treatment effect as assessed by BCVA at day 90 was thus supported by this anatomical finding. By day 180, the mean retinal thickness reduction (−119.3 μm) compared with control was not significant.

Patients who had a BCVA score of <84 OR retinal thickness >250 μm by optical coherence tomography OCT and in the investigator's opinion treatment would not put the patient at risk were eligible to receive a Dexamethasone Implant treatment in an open label extension. Of the patients who were treated in the open label phase, 98% received a Dexamethasone Implant injection between 5 and 7 months after the initial treatment.

As for the initial treatment, peak response was seen at day 60 in the open label phase. The cumulative response rates were higher throughout the open label phase in those patients receiving two consecutive Dexamethasone Implant injections compared with those patients who had not received an injection in the initial phase.

The proportion of responders at each time point was always greater after the second treatment compared with the first treatment. Whereas, delaying treatment for 6 months results in a lower proportion of responders at all time points in the open label phase when compared with those receiving a second injection.

A total of 47.3% of patients experienced at least one adverse reaction. The most frequently reported adverse reactions in patients who received the Dexamethasone Implant were increased intraocular pressure (24.0%) and conjunctival hemorrhage (14.7%). The adverse reaction profile for BRVO patients was similar to that observed for CRVO patients, although the overall incidence of adverse reactions was higher for the subgroup of patients with CRVO. Other common adverse reactions recorded were headache, vitreous detachment, cataract and subcapsular cataract, as well as visual disturbance. Additional common adverse reactions considered to be related to the injection procedure rather than the Dexamethasone Implant were the occurrence of vitreous hemorrhage, vitreous opacities (including vitreous floaters), eye pain, photopsia, conjunctival edema, and conjunctival hyperemia.

Increased intraocular pressure (IOP) with the Dexamethasone Implant peaked at day 60 and returned to baseline levels by day 180. Elevations of IOP either did not require treatment or were managed with the temporary use of topical IOP-lowering medicinal products. During the initial treatment period, 0.7% (3/421) of the patients who received the Dexamethasone Implant required laser or surgical procedures for management of elevated IOP in the study eye compared with 0.2% (1/423) with control.

The adverse reaction profile of 341 patients analyzed following a second injection of the Dexamethasone Implant was similar to that following the first injection. A total of 54% of patients experienced at least one adverse reaction. The incidence of increased IOP (24.9%) was similar to that seen following the first injection and likewise returned to baseline by open label day

180. The overall incidence of cataracts was higher after 1 year compared to the initial 6 months (Ozurdex Summary of Product Characteristics 2013).

Efficacy and Safety in Uveitis

The clinical efficacy of the Dexamethasone Implant has been assessed in a single, multicenter, masked, randomized study for the treatment of noninfectious ocular inflammation of the posterior segment in patients with uveitis. A total of 229 patients were randomized to receive dexamethasone 350 μg or 700 μg implants or sham. Of these, a total of 77 were randomized to receive Dexamethasone 700 μg Implant, 76 to dexamethasone 350 μg, and 76 to control (sham injections). A total of 95% of patients completed the 26-week study.

The proportion of patients with vitreous haze score of 0 in the study eye at week 8 (primary endpoint) was fourfold higher with the Dexamethasone 700 μg Implant (46.8%) compared to control (11.8%), $p < 0.001$. Statistical superiority was maintained up to and including week 26 ($p \leq 0.014$).

The cumulative response rate curves (time to vitreous haze score of 0) were significantly different for the Dexamethasone 700 μg Implant group compared to the control group ($p < 0.001$), with patients receiving dexamethasone showing an earlier onset and greater treatment response.

The reduction in vitreous haze was accompanied by an improvement in visual acuity. The proportion of patients with at least 15 letters improvement from baseline BCVA in the study eye at week 8 was more than sixfold higher with Dexamethasone 700 μg Implant (42.9%) compared to control (6.6%). Statistical superiority was achieved at week 3 and maintained up to and including week 26 ($p < 0.001$).

The percent of patients requiring escape medications from baseline to week 8 was nearly threefold less with the Dexamethasone 700 μg Implant (7.8%) compared to control (22.4%) ($p = 0.012$).

The most frequently reported adverse reactions in the study eye of patients who received Dexamethasone 700 μg Implant were conjunctival hemorrhage (30.3%), increased intraocular pressure (25.0%), and cataract (11.8%). Other commonly observed adverse reactions were retinal detachment, myodesopsia, vitreous opacities, blepharitis, eyelid pruritis, and visual impairment. Adverse reactions considered to be related to the injection procedure were abnormal sensation in the eye as well as sclera hyperemia (Ozurdex Summary of Product Characteristics 2013).

Efficacy and Safety in Diabetic Macular Edema (DME)

The use of the Dexamethasone 700 μg Implant in patients suffering from diabetic macular edema (DME) was initially approved in patients who have an artificial lens as well as patients with a natural lens, but scheduled for cataract surgery. However, the FDA subsequently expanded the label to include all patients with DME with the only restriction being those eyes with a torn or ruptured posterior capsule. Data from the following major trials has so far been published: Haller and colleagues compared the Dexamethasone Implant (in two concentrations: 350 μg or 700 μg) to no treatment. The implants were inserted through a 20 gauge transscleral incision. The study included a total of 171 patients. At day 90, the group with the Dexamethasone 700 μg Implant showed a statistically significantly proportion of patients with a 10 or more letter gain compared to no treatment (33% vs. 12%, $p = 0.007$). Mean central macular thickness (CMT) was reduced by 132.27 μm (SD 160.86) from baseline in the Dexamethasone 700 μg Implant group, which was statistically significant compared to no treatment ($p > 0.001$). An increased IOP was recorded in 9.4% of cases in the Dexamethasone 700 μg Implant group (compared to 14.5% of cases having received the 350 μg implant).

Another trial recorded the efficacy of the Dexamethasone 700 μg Implant in combination with laser compared to laser as monotherapy ($n = 253$). A significantly greater improvement in mean best corrected visual acuity (BCVA) was seen during the first 9 months in the group receiving the implant followed by laser

photocoagulation after 1 month compared to laser only treatment ($p < 0.05$). A mean of 1.6 implants were used over a period of 12 months. At months 1 and 6 the combination group also had significantly greater mean reductions from baseline in CMT ($p < 0.001$). An elevated IOP was found in 20% of patients in the combination group (compared to only 1.6% in the laser group), but only 1% of patients experienced an IOP elevation of more than 10 mmHg (Ford et al. 2013).

Additionally, results from a multicenter, randomized clinical study assessing the efficacy and safety of Dexamethasone Implants (700 or 350 μg) compared with control in 1,048 patients were reported recently. All three treatment groups were followed for a period of 3 years. The mean number of implants received was 4.1, 4.4, and 3.3 with the Dexamethasone 700 μg Implant, the Dexamethasone 350 μg Implant, and the control (sham), respectively. At study end, the percentage of patients with an improvement of 15 or more letters was greatest in the group with the Dexamethasone 700 μg Implant (22.2% vs. 18.4% and vs. 12% with $p \leq 0.018$). The mean reduction of central retinal thickness (CRT) was also greatest in this group (111.6 vs. 107.9 μm and vs. 41.9 μm with $p < 0.001$). Rates of cataract related adverse events in phakic eyes were 67.9%, 64.1%, and 20.4% in the three respective groups. Increases in IOP were usually controlled with medication or no therapy. Only two patients (0.6%) in the Dexamethasone 700 μg Implant group and one patient (0.3%) in the Dexamethasone 350 μg Implant group required trabeculectomy. These results confirmed the efficacy endpoints of the study, while the safety profile was considered acceptable and consistent with previous reports (Boyer et al. 2014).

Furthermore, real world results from a retrospective analysis were also recently published. In this study charts from 74 patients suffering from DME who had received the Dexamethasone 700 μg Implant and had been followed-up for a minimum of 6 months were evaluated. Values from month 2 and 6 after injection of the implant were reported. While the average CRT decrease was 239 μm and 135 μm at month 2 and 6, respectively, a gain greater than 15 letters in BCVA was found in 27% of patients at month 6. The mean rate of injections was 1.2 at month 6, with an average of 5.4 months to reinjection. Ocular hypertension greater than 25 mmHg was observed in 13.4% of patients and managed solely by topical treatment (Guigou et al. 2014).

Summary and Conclusion

The Dexamethasone 700 μg Implant has already successfully passed the regulatory hurdle for treatment of ME secondary to CRVO and BRVO as well as for management of uveitis, and most recently for DME. For all indications the effect of the Dexamethasone 700 μg Implant in terms of improvement of the patient's VA as well as reduction of CRT is significant when compared to control. Until now there are hardly any large and well planned trials directly comparing the Dexamethasone 700 μg Implant with other existing intravitreal treatments. Overall, steroids act broadly against inflammatory molecules, reducing not only VEGF but many other angiogenic and inflammatory cytokines involved in the formation of edema and leakage.

An additional advantage of the Dexamethasone Implant is its slow release mechanism, enabling the treating physician to manage the patient with fewer overall injections compared to alternative existing treatments without sustained release approaches. This implies that injection-related side effects are minimized.

Dexamethasone is a well-know compound that has been used for many years in a plethora of different indications, administration routes, and dosages. Side effects such as cataract formation and elevation of IOP are well documented. However, especially for the latter, it seems that this new intravitreal route does not cause a significant number of unmanageable rises in IOP.

In conclusion, the Dexamethasone Implant appears to be a useful addition to the currently limited existing armamentarium of treatments for ME secondary to RVO and DME as well as uveitis.

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DFB

▶ Desferrioxamine Retinopathy

DFOA

▶ Desferrioxamine Retinopathy

DFO-B

▶ Desferrioxamine Retinopathy

Diabetic Disc Edema

▶ Diabetic Papillopathy

Diabetic Macular Edema

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Synonyms

Center-involved diabetic macular edema; Clinically significant macular edema (CSME); DME

Definition

Diabetic macular edema (DME) is retinal thickening within the posterior pole that is attributed to diabetes mellitus. It may be recognized on stereoscopic fundus biomicroscopic examination, stereoscopic fundus photography, and/or ocular coherence tomography (OCT).

Epidemiology

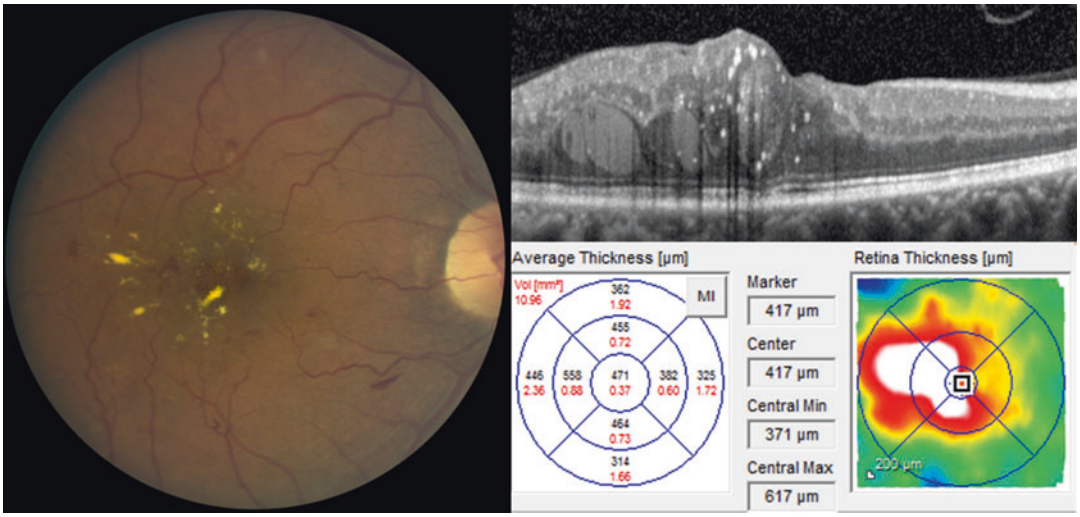
From 1980 through 2014, the number of US adults aged 18 years or older diagnosed with diabetes has risen dramatically, from 5.5 million to 21.9 million (CDC 2015). Despite advances in the treatment of diabetes and in diabetes-related eye disease, diabetic macular edema and complications related to diabetic retinopathy remain the leading causes of vision loss and new-onset visual impairment in working-age adults in the United States (Cheung et al. 2010).

Etiology

DME is a multifactorial condition in which hyperglycemia is associated with vascular hyperpermeability and inflammation. Chronic elevation in blood glucose promotes pericyte dropout and loss of capillary integrity, retinal hypoxia, and upregulation of multiple pro-inflammatory cytokines and chemokines (Das et al. 2015). Vascular endothelial growth factor (VEGF), a potent pro-permeability cytokine and mediator of angiogenesis, is found in elevated concentrations in the diabetic retina and promotes inflammation and retinal vascular leakage. VEGF, in concert with other vasoactive mediators, matrix metalloproteinases, pro-adhesion molecules, reactive oxygen species, and sorbitol, contributes to a positive feedback loop, causing further endothelial compromise, inflammation, and vascular permeability (Augustin et al. 2010). Leakage of plasma into the retina leads to DME.

Clinical Presentation

Patients with center-involving DME (CI-DME) have retinal thickening that involves the foveal center. These individuals may present with blurred central vision and metamorphopsia, or they may not recognize any symptoms. As a generality, the degree of vision impairment associated with CI-DME correlates with the severity of foveal thickening as measured on OCT, but the magnitude of this correlation has varied widely between studies ranging from low to high correlation indices (DRCR et al. 2007). It is possible for patients to present with relative preservation of central visual acuity and the absence of symptoms despite marked central macular thickening (Fig. 1), as well as the converse; there may be



Diabetic Macular Edema, Fig. 1 Best-corrected visual acuity is 20/25 in this eye of a 45-year-old man who denies any vision symptoms, despite center-involved diabetic macular edema. The central subfield thickness on OCT is moderately thickened at 471 um, and there is a moderate amount of juxtafoveal intraretinal lipid and intraretinal hemorrhages

moderate compromise in visual acuity with mild macular thickening. The latter may be due to chronic DME that has led to irreversible loss of neurosensory retinal tissue with or without atrophic retinal pigment epithelial (RPE) changes. Patients may also be aware of color vision compromise, poor night vision, or poor dark–light adaptation (Danis 2008). DME may be present at any point along the spectrum of nonproliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR).

Diagnosis

Stereoscopic fundus biomicroscopy performed with direct contact lens or indirect lens (+78 or +90 diopter) facilitates identification of retinal thickening. OCT is a rapid, noninvasive imaging modality that has become the most commonly utilized imaging tool to confirm the presence of DME or identify subclinical DME (retinal thickening, two standard deviations beyond average normal thickness that is not appreciated on clinical examination). OCT provides both qualitative and quantitative data to characterize DME. Severity (degree of thickening), location (central, inner, and outer subfield involvement within a 6-mm diameter zone centered on the fovea), and accompanying retinal features (intraretinal lipid, cystoid abnormalities, and RPE abnormalities) can be monitored for disease evolution and response to treatment. Although the Early Treatment Diabetic Retinopathy Study (ETDRS) previously offered a definition of clinically significant diabetic macular edema (CSME), this classification predated OCT and is largely being replaced by OCT identification of retinal thickening that is described as center-involving (central DME) or non-center-involving DME. Gender and instrument-specific thresholds to classify the eyes as manifesting center-involved DME have been published. Historically, CSME was defined on clinical exam or stereoscopic color fundus photographs as (1) thickening of the retina at or within 500 μm of the center of the macula; (2) hard exudates at or within 500 μm of the center of the macula, if associated with thickening of the adjacent retina; or (3) a zone of retinal thickening $\geq$1 disk area, any part of which lies within 1-disk diameter of the center of the macula (ETDRS Research Group 1985). Fluorescein angiography (FA) may also be helpful in the evaluation of DME, in that FA frequently identifies the source of leakage responsible for the DME, namely, microaneurysms and dilated capillaries. FA provides a road map of potential targets when and if focal/grid laser photocoagulation is considered in the treatment plan. FA also assists in identification of areas of macular ischemia which may be helpful to determine the mechanism of vision compromise in patients with diabetic retinopathy.

Differential Diagnosis

The differential diagnosis for DME includes other retinal vascular diseases that may also be associated with vascular leakage and macular thickening and/or intraretinal lipid. Some of the more common entities within the differential diagnosis would include branch or central retinal vein occlusion, idiopathic juxtafoveal telangiectasia, hypertensive retinopathy, radiation retinopathy, ruptured retinal macroaneurysm, and pseudophakic cystoid macular edema.

Predictive Factors for Incident DME

The risk of developing DME is similar to the risk of developing diabetic retinopathy (DR) in general. Well-known risk factors for DME and DR among persons with DM include longer duration of diabetes, post-puberty, and pregnancy. No genetic association has been reported for the development of DME (Das et al. 2015). Non-Hispanic black race, longer duration of diabetes, and higher levels of hemoglobin A1C were associated with greater prevalence of DME in cross-sectional multivariate regression analysis within the National Health and Nutrition Examination Survey (NHANES) (Varma et al. 2014).

Hyperglycemia is the most important modifiable risk factor associated with the development

of DME. Both the Diabetes Control and Complications Trial (DCCT, Type 1 DM) and the UK Prospective Diabetes Study (UKPDS, Type 2 DM) showed that tight glycemic control (hemoglobin A1C < 7%) reduces the risk of developing and having progression of DR (DCCT Group 2000; UKPDS 1999). In addition, at the final DCCT visit (mean follow-up of 6.5 years), tight control reduced the prevalence of CSME when compared to conventional control (3.8% vs. 6.8%, $p = 0.02$) (DCCT et al. 2015). The Epidemiology of Diabetes Interventions and Complications (EDIC) study extended the follow-up on the DCCT participants for up to an additional 18 years from closeout of the DCCT. Throughout EDIC, the prevalence of DME continued to increase in each group, and tight control continued to reduce the prevalence of CSME through the EDIC 10-year exam (9.4% vs. 20.4%, $p = 0.004$, tight vs. conventional control, 95% CI). As the level of glycemic control in the two treatment arms became more similar during EDIC, approximately 8% in each group (compared to the treatment group differences during the DCCT, about 7% vs. 9%), the probability of developing new CSME became similar between the two groups during the interval between the 10- and 15–18-year EDIC visits. These findings highlight the long-term benefits of better control early on in the course of these individuals but also emphasize that there is a limit to this favorable metabolic memory.

The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) is a large population-based study which reexamined a cohort of persons with diabetes 10 years after their initial examination. Ten-year incidence rates of CSME ranged from 8% to 18% depending on insulin use and age at DM diagnosis. Among the younger and older onset study participants, the higher the glycosylated hemoglobin at the baseline examination, the higher the incidence of macular edema at the 10-year visit (OR = 1.56 for each Hgb A1c%, 95% CI, 1.38, 1.76; OR = 1.65, 95% CI, 1.42–1.92 younger/older onset participants, respectively). Incident DME also was higher among those with a greater increase in their glycosylated hemoglobin between the baseline and the 4-year visit (18–37% increase per % point increase depending on age at DM onset). In all participants incident macular edema increased significantly with increasing severity of baseline retinopathy level ($P < 0.0001$). These findings suggest that a sustained reduction in hyperglycemia may result in a beneficial reduction in incident macular edema (Klein et al. 1995).

Associations between development of DME and dyslipidemia have been inconsistent. There is no current evidence that intensive control of dyslipidemia by statin agents is useful in treating or preventing DR or DME (Lee et al. 2015). Prophylaxis for DME and DME-related vision loss is best accomplished by tight glycemic control and early and regular retinal examination of individuals with diabetes.

Therapy

Focal/Grid Photocoagulation

Prior to 2010, the gold standard therapy for management of DME was focal/grid photocoagulation. Laser photocoagulation may be applied directly to microaneurysms (focal treatment) and in a grid pattern to areas of leaking capillaries, each confined to areas of retinal thickening. The mechanism by which focal/grid laser leads to reduction in anatomic DME is not completely understood. The ETDRS concluded that focal/grid laser was safe and effective in reducing vision loss in eyes with CSME from diabetes (ETDRS 1985, 1991). Patients with CSME and less severe (mild or moderate) NPDR randomly assigned to the immediate focal/grid laser group were less likely to experience moderate vision loss (loss of 15 or more letters) than those assigned to the deferred laser (deferral of focal laser) group (12% immediate focal vs. 24% delayed focal at 3 years). Although laser treatment has been able to limit vision loss in eyes with DME, it seldom is associated with vision improvement. Among the subgroup of eyes in the ETDRS with center-involving DME and vision impairment of 20/40 or worse, at 3 years about 40% of the immediate focal/grid laser group had a six or more letter improvement in ETDRS letter score compared

with approximately 20% of the deferred treatment group (ETDRS 1985). Less than 3% of patients achieved visual improvement of at least 15 letters in each of the subgroups. Focal/grid laser often requires more than one application, but it is generally well tolerated and has a low complication rate which includes potential inadvertent foveal burns, paracentral scotomas, choroidal neovascularization, laser scar expansion over time (so-called laser creep), vitreous hemorrhage, subretinal fibrosis, and migration of intraretinal lipid into the fovea. Focal/grid laser is still in use, but it may no longer be a first-line therapy for CI-DME when access to pharmacologic agents is available. More typically, its present use is reserved for non-central diabetic edema. Among patients with CI-DME, it may be used among those for whom intravitreal injections are contraindicated or for those who will not accept intravitreal medications and the frequent visit schedule needed to deliver this treatment. It also still has a role as an adjuvant therapy in eyes receiving intravitreal medications to manage DME.

Vitrectomy

Vitrectomy with or without the removal of the internal limiting membrane (ILM) has been utilized in the treatment of DME. Vitrectomy may increase oxygen tension within the vitreous cavity, promoting constriction of retinal arterioles, leading to decreased vascular hydrostatic pressure in capillaries and venules, and resultant decreased edema (Stefansson 2001). Increased oxygen tension may also reduce production of VEGF. Further, vitreomacular traction may contribute to or exacerbate DME, and this can be anatomically altered with surgery. A Diabetic Retinopathy Clinical Research (DRCR) network protocol followed a cohort of 87 eyes for 1 year following vitrectomy surgery to manage DME and vitreomacular traction (DRCR 2010). Preoperative visual acuity was a median of 20/100 (range 20/63–20/400). The method of vitrectomy was at the surgeon's discretion and may or may not have incorporated adjunctive intravitreal steroid, focal/grid laser photocoagulation, or ILM peeling. At 6 months, 68% of eyes showed a reduction in the median central subfield thickness by ≥50% on OCT, but only 38% of eyes showed improvement in ETDRS letter score of ten or more letters.

Pharmacotherapy

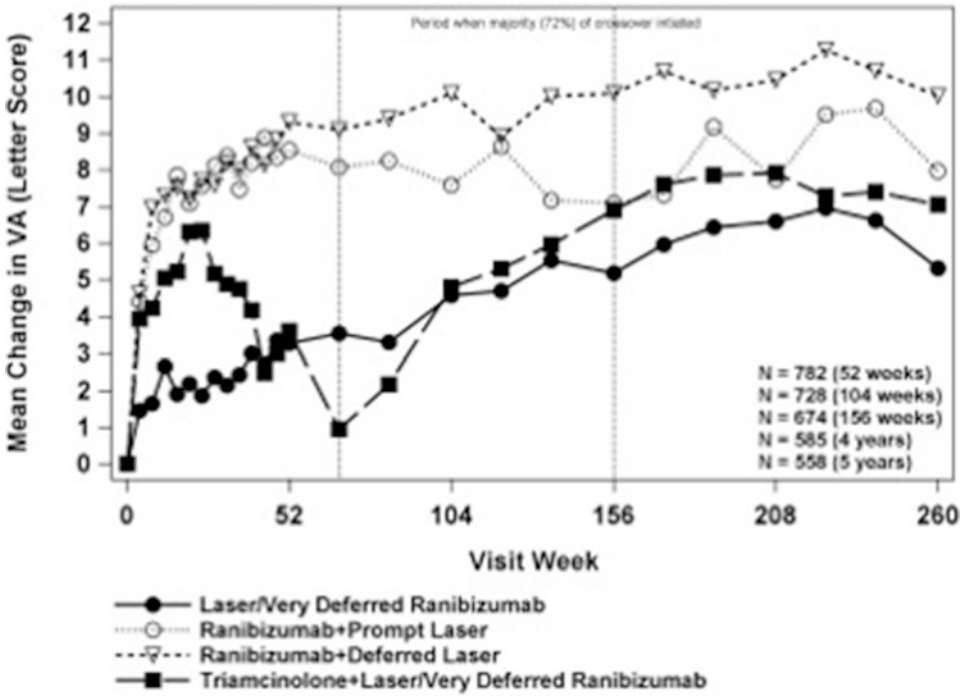
Anti-vascular Endothelial Growth Factor Therapy

Anti-VEGF is the current first-line therapy for CI-DME. Several anti-VEGF-A agents have been evaluated in the treatment of DME. Some of the pivotal clinical trials that have established the efficacy of anti-VEGF agents over previous management strategies are summarized below.

Ranibizumab (Lucentis, Genentech, South San Francisco, CA), a monoclonal antibody that blocks all isoforms of VEGF-A, has been proven effective in the management of DME as it restores DME-related vision loss in many and prevents further vision loss in the majority of eyes receiving this therapy. The DRCR.net protocol I (the Laser–Ranibizumab–Triamcinolone Study) study enrolled 854 eyes with center-involving DME (confirmed with time-domain OCT central subfield thickness >250 μm) and vision impairment of 20/32–20/320 (Elman et al. 2011). Patients were randomly assigned to sham injection plus prompt laser, intravitreal ranibizumab 0.5 mg plus prompt laser, intravitreal ranibizumab 0.5 mg plus deferred (≥24 weeks) laser, or intravitreal triamcinolone 4 mg plus prompt laser. The mean change in visual acuity between baseline and the 1-year visit (the primary outcome of the study) was +3 letters in the sham plus prompt laser group, compared with +9 letters in the ranibizumab plus prompt laser ($P < 0.001$) or ranibizumab plus deferred laser group ($P < 0.001$). Follow-up of the ranibizumab groups through 5 years has shown the stability of this outcome (Bressler et al. 2016). The proportions of eyes experiencing a 10–14-letter improvement and those improving 15 or more letters from baseline were 16% and 32% in the ranibizumab plus prompt laser group and 16% and 37% in the ranibizumab plus deferred laser group. The rates of at least a ten-letter loss were each only 3% in the respective ranibizumab groups. The rapid rise in mean change in visual acuity that

occurred in the initial 6 months of follow-up was accompanied by a simultaneous rapid reduction in central subfield thickness (CST). The mean decrease in CST was 174 μm in the sham plus laser group compared with 225 μm in the ranibizumab plus prompt laser group ($P < 0.001$) and 226 μm in the ranibizumab plus deferred laser group ($P < 0.001$) at 1 year. While applying the structured re-treatment protocol (based on changes in CST and VA), the cumulative injection number was 8 in the ranibizumab plus prompt laser group and 9 in the ranibizumab plus deferred laser groups in the first year of the study. Between the 1- and 2-year visits, the median number of injections fell dramatically to 2 and 3 and remained 0–1 for years 3, 4, and 5. In contrast to managing neovascular age-related macular degeneration with anti-VEGF therapy, when one is managing DME, it is apparent the anti-VEGF treatment burden decreases after the first year of treatment, while visual gains and reductions in central retinal thickness are maintained through 5 years (Fig. 2) (Bressler et al. 2016).

The RISE and RIDE trials, two parallel, randomized, phase 3 studies, also demonstrated superior visual outcomes among eyes treated monthly with 0.3-mg or 0.5-mg intravitreal ranibizumab compared with those in the control arm (sham injections, focal/grid laser permitted but not required beginning at month 3) (Brown et al. 2013). In RISE the mean change in VA letter score between baseline and the 2-year visit in the sham, 0.3-mg ranibizumab and 0.5-mg ranibizumab groups, was +2.6, +12.5, and +11.9 letters, respectively ($P < 0.001$ for each ranibizumab comparison to sham), while in the RIDE trial, the same outcomes were +2.3, +10.9, and +12 letters, respectively ($P < 0.001$ for each ranibizumab comparison to sham). At 2 years in the RISE study, 18% of sham participants gained at least 15 letters vs. 45% of 0.3-mg ($P < 0.0001$)



Diabetic Macular Edema, Fig. 2 Mean change in visual acuity letter score over 5 years from a randomized trial comparing ranibizumab with prompt or deferred laser, laser with deferred ranibizumab, and triamcinolone plus deferred ranibizumab in eyes with vision impairment from center-involving DME (Reprinted with permission, Bressler et al. 2016. American Journal of Ophthalmology, volume 164, 2016, 57–68)

and 39% of 0.5-mg ranibizumab group ($P < 0.001$). Similarly, at 2 years In RIDE, significantly more ranibizumab-treated patients gained 15 letters or more: 12% of sham eyes vs. 34% of 0.3-mg eyes ($P < 0.0001$) and 46% of 0.5-mg eyes ($P < 0.0001$). Reductions in CST paralleled the rise in VA in the ranibizumab eyes, with greater reductions in CST among the ranibizumab groups relative to the control arm (mean decrease in CST ranged from 251 to 271 μm in the ranibizumab groups and 126–133 μm in the control group at 24 months).

In addition to protocol I, RIDE and RISE also provided data demonstrating low rates of both ocular and systemic adverse events in all treatment groups; in particular no increase in thromboembolic events (events described by the Antiplatelet Trialists' Collaboration) occurred in the ranibizumab groups compared to the control arms. In addition, all three studies provided exploratory evidence that eyes managed with ranibizumab were more apt to have improvement in the severity of their retinopathy level (regression of disease) and slower progression or worsening of retinopathy compared with the control groups.

Bevacizumab (Avastin, Genentech, South San Francisco, CA) is a full-length monoclonal antibody that blocks all isoforms of VEGF-A. Bevacizumab is a commonly used "off-label" in the management of DME. The bevacizumab or laser therapy (BOLT) trial compared intravitreal bevacizumab to focal/grid laser (Rajendram et al. 2012). Among the 65 patients enrolled in this study, the 28 eyes randomly assigned to laser had a mean change of −0.5 letters in their ETDRS letter score at month 24, while the 37 eyes assigned to repeated intravitreal bevacizumab every 6 weeks showed a mean change of +8.6 letters at the same time point ($P = 0.005$). At 24 months, more eyes gained ≥10 letters and ≥15 letters in the bevacizumab group than the laser group (49% vs. 7%, $P = 0.001$, and 32% vs. 4%, $P = 0.004$, respectively). While no bevacizumab-treated eyes lost ≥15 letters, 14% did so in the laser group ($P = 0.03$).

Aflibercept (Eylea, VEGF-Trap Eye, Regeneron, Tarrytown, NY), another VEGF-A antagonist, is a soluble protein which contains the extracellular VEGF receptor 1 and 2 sequences fused to the Fc domain of a human immunoglobulin-G1 molecule. Aflibercept has 100-fold greater binding affinity to VEGF than either ranibizumab or bevacizumab (Das et al. 2015). In addition, aflibercept blocks all isoforms of placental growth factor, a substance which may also contribute to vascular permeability and retinal neovascularization. The VIVID and VISTA trials were two parallel phase 3 trials which compared two different aflibercept-dosing regimens to focal/grid laser (Brown et al. 2015). Eyes were randomly assigned to aflibercept 2 mg every 4 weeks (2q4), aflibercept 2 mg every 8 weeks after 5 monthly doses (2q8), or focal/grid laser. Mean change in ETDRS VA letter score from baseline to week 100 in the aflibercept 2q4 and 2q8 groups were +11.5 and +11.1 compared with +0.9 in the laser group in VISTA ($P < 0.0001$ for each aflibercept regimen compared to control) and +11.4, +9.4, and +0.7 letters, respectively, in VIVID ($P < 0.0001$ for each aflibercept regimen compared to control). The proportion of eyes that improved by ≥15 letters at week 100 was 38% (2q4), 33% (2q8), and 13% (focal/grid) in VISTA and 38%, 31%, and 12%, respectively, in VIVID ($P < 0.0001$ for each aflibercept comparison to laser for both studies). The proportion of eyes that lost ≥15 letters at week 100 also statistically favored aflibercept with rates of 3.2% (2q4) ($P = 0.022$), 0.7% (2q8) ($P < 0.001$), and 9.7% (focal/grid) in VISTA and 2.2% (2q4) ($P < 0.001$) and 1.5% (2q8) ($P < 0.001$) compared to 12.9% (focal/grid) in VIVID. Exploratory analyses from these trials also found significantly more eyes in the aflibercept groups vs. those in the laser group who had a ≥2 step improvement in the ETDRS retinopathy level in both VISTA and VIVID.

Given the Level 1 evidence supporting efficacy and safety of each of the presently available anti-VEGF agents to manage DME, the DRCR.net

protocol T performed a comparative efficacy trial of ranibizumab, bevacizumab, and aflibercept in eyes with CI-DME and vision impairment (DRCR et al. 2015, 2016). In eyes with CI-DME and relatively good vision (20/32 or 20/40), all three drugs were effective in achieving a mean improvement of about eight letters in ETDRS letter score at 1 year, which was maintained through the 2-year visit. Aflibercept, however, outperformed ranibizumab 0.3- and 1.25-mg bevacizumab among eyes that presented with vision impairment of 20/50–20/320. In this cohort, from baseline to 1 year, the mean improvement in VA letter score was +13.3 letters with aflibercept, +9.7 letters with bevacizumab (aflibercept–bevacizumab, $P < 0.001$), and +11.2 with ranibizumab 0.3 mg (aflibercept–ranibizumab, $P = 0.03$, ranibizumab–bevacizumab, $P = 0.21$). At 2 years, in the subgroup of eyes with lower baseline VA (20/50–20/320), the mean change in VA was +18.1, +13.3, and +16.1 letters, in the aflibercept, bevacizumab, and ranibizumab groups, respectively. Only the aflibercept–bevacizumab comparison remained significant ($P = 0.02$). At the 2-year visit, OCT CST decreased on average ($\pm SD$) by 171 ± 141 μm with aflibercept, 126 ± 143 μm with bevacizumab, and 149 ± 141 μm with ranibizumab (aflibercept vs. bevacizumab, −48.5 μm, $P < 0.001$; aflibercept vs. ranibizumab, −15.5 μm, $P = 0.08$; and ranibizumab vs. bevacizumab, −33 μm, $P < 0.001$). Focal/grid laser was required if CI-DME persisted and was no longer showing successive improvement following six consecutive injections. Eyes assigned to bevacizumab were most apt to receive laser (64%), followed by ranibizumab (52%), while the aflibercept eyes were less likely to need laser (41%) ($P < 0.001$). In all treatment groups, the number of injections needed in the second year was about half the number required in the first year with a cumulative median number of about 15 injections in all groups. Antiplatelet Trialists' Collaboration (APTC) events occurred in 5% with aflibercept, 8% with bevacizumab, and 12% with ranibizumab ($P = 0.34$ for aflibercept vs. bevacizumab, $P = 0.047$ for aflibercept vs. ranibizumab, and $P = 0.20$ for ranibizumab vs. bevacizumab). The significance of this observation is unclear as it is inconsistent with other studies to date.

Steroids

As many inflammatory mediators have been implicated in the pathogenesis of DME and diabetic retinopathy, it follows that steroids may have a role in the management of DME. Cataract formation and elevation of intraocular pressure are two drug-related adverse events, seen with varying frequency depending on the specific steroid preparation, that limit the use of intraocular steroids in DME management, often relegating these agents to second-line therapy.

The DRCR.net protocol B found that 4-mg intravitreal triamcinolone was no better than focal/grid laser at altering vision outcomes at 2 (DRCR 2008; Elman et al. 2011). Similarly, in the DRCR protocol I, eyes randomly assigned to 4-mg intravitreal triamcinolone plus prompt laser did not experience superior vision outcomes relative to the sham plus prompt laser group at 1 year (Elman et al. 2011). However, in a subgroup analysis of eyes that were pseudophakic at baseline ($n = 273$), the triamcinolone plus prompt laser group had a mean change of +8 letters which appeared comparable to the two ranibizumab groups at 1 year. However, by the year 5 visit, the pseudophakic subgroup assigned to triamcinolone plus prompt laser did not appear to maintain this level of improvement (Bressler et al. 2016).

The MEAD study randomly assigned 1048 eyes with CI-DME and vision of 20/50–20/200 to 0.7-mg or 0.35-mg dexamethasone intravitreal implant (Ozurdex; Allergan, Inc., Irvine, CA) or sham injections (Boyer et al. 2014). Only 58% (607/1048) completed the 3-year trial, limiting the interpretation of the results. Some eyes experienced vision improvement, while others lost vision. Cataract formation and steroid-related elevations in intraocular pressure were observed.

Another intravitreal steroid implant, the fluocinolone acetonide implant, was evaluated in the FAME trial (Campochiaro et al. 2011). Study eyes had persistent DME (CI-DME that persisted despite one or more prior focal/grid laser treatments) and were randomly assigned to 0.2 μg/day or 0.5 μg/day fluocinolone acetonide implants or sham injections. The mean improvement in VA letter score between baseline and the 2-year visit was +4.4 letters in the 0.2-μg implant and +5.4 letters in the 0.5-μg implant group compared with +1.7 letters in the sham group ($P = 0.02$ and $P = 0.016$). One subgroup appeared to benefit more than others, which were eyes with DME duration greater than 3 years at study entry. In this subgroup, 34% of the 0.2-μg ($P < 0.001$) and 29% of the 0.5-μg group ($P = 0.002$) had at least a 15-letter improvement compared with 13% of the sham group.

The FAME study did allow treatments other than the random assignment if CI-DME persisted, and more eyes in the implant group avoided focal/grid laser compared to the sham group (63–65% in the implant groups compared with 41% in the sham group). Similarly more eyes in the sham group (29%) received alternative rescue treatments for DME (which may have included anti-VEGF therapy) than those in the low-dose (13%) or high-dose (14%) implant groups. Elevated intraocular pressure-requiring incisional glaucoma surgery was reported in 8% of patients in the 0.5-μg group and 4% in the 0.2-μg group. Almost all phakic patients in the implant groups developed visually significant cataract. Following cataract surgery, eyes that had been phakic at baseline but assigned to the implant groups demonstrated similar visual benefit compared to eyes that were pseudophakic at study entry.

Future Therapies

Several large clinical trials have established anti-VEGF agents as current first-line therapy for CI-DME treatment. However, some patients may not be able to comply with the frequent visits that are needed in the first few years of therapy in order to realize the benefits of this treatment. Some eyes will manifest persistent CI-DME despite receiving regular anti-VEGF therapy with long-term vision outcomes that may not be as robust as what occurs among eyes that anatomically respond with time (Bressler et al. 2016). Therefore, research continues into alternative treatment strategies.

The use of steroid medications in combination with anti-VEGF therapy is being studied as a strategy to further improve visual outcomes while decreasing treatment burden in DME patients. Longer-acting anti-VEGF agents administered by way of sustained drug delivery systems are also being evaluated as potential DME treatments.

Designed ankyrin repeat proteins (DARPins), proteins with high-affinity binding for VEGF administered by intravitreal injection, are in early phase 3 testing as another potential therapy for DME (Agarwal et al. 2015; Das et al. 2015). Vascular adhesion protein-1 (VAP-1) inhibitors, insulin-like growth factor inhibitors, interleukin inhibitors, chemokine inhibitors, and inhibitors of the angiopoietin/TIE-2 pathway are all in various phases of early investigation as novel therapies in DME, as is sirolimus, an inhibitor of various pro-inflammatory cytokines and inflammatory-associated genes (Das et al. 2015).

Prognosis

The prognosis for maintenance of good vision is more favorable if DM is diagnosed and controlled early in its course. With regular monitoring of glycemic control and regulation of modifiable systemic risk factors by the medical team, coupled with consistent retinal exams, individuals with DM are far less likely to experience significant vision loss from DME. Prognosis for visual acuity among those individuals that do develop DME is very good in the present era of anti-VEGF therapy. Large clinical trials demonstrate that eyes that present with a better level of visual acuity when initiating therapy are most apt to maintain the best level of acuity in follow-up. This emphasizes the need for regular surveillance examinations to detect DME early in its course before greater levels of vision impairment occur.

Cross-References

- Aflibercept
- Bevacizumab
- Clinically Significant Macular Edema (CSME)
- Diabetic Retinopathy
- Focal Grid Laser
- Ranibizumab

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Diabetic Optic Neuropathy

► Diabetic Papillopathy

Diabetic Papillitis

► Diabetic Papillopathy

Diabetic Papillopathy

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Synonyms

Diabetic disc edema; Diabetic papillitis; Diabetic optic neuropathy

Definition

Diabetic papillopathy (DP) describes unilateral or more commonly bilateral optic disc edema with variable visual loss seen in diabetic patients. DP can occur in both type 1 and type 2 diabetes mellitus. Some authors believe that DP is a separate nosologic entity, while others believe it is on the spectrum of nonarteritic anterior ischemic optic neuropathy (NAION) in a diabetic patient.

Etiology

The precise pathogenesis of DP is not known and there is no direct relationship between the metabolic control of the diabetes and the presence or stage of diabetic retinopathy. Though diabetic microangiopathy has been proposed by some as a possible etiology, no pathologic studies of DP have been performed. Thus, many authors argue that DP is in fact a milder form of NAION. Both NAION and DP share the following features: diabetes as a risk factor, a small optic cup/crowded optic nerve head (i.e., the "disc at risk"), nerve fiber layer defects, and subsequent sector or diffuse optic disc pallor. On the other hand, there are some differences that have been proposed to differentiate DP from NAION: the disc edema of NAION usually resolves within 3 months, whereas a length of up to 10 months or longer is common in DP; DP also tends to more commonly affects younger age groups and is more often bilateral than NAION, and the disc appearance may have more prominent telangiectasias in DP than NAION.

Clinical Presentation

The presentation of DP can mimic "garden variety" NAION with ipsilateral visual acuity or visual field loss; a relative afferent pupillary defect (if unilateral or bilateral but asymmetric), concomitant vasculopathic risk factors, a fellow eye with the structural "disc at risk"; and optic disc edema that eventually becomes optic atrophy. There may also be concomitant diabetic retinopathy and/or diabetic macular edema but this is quite variable.

Diagnostics

If bilateral disc edema is present, potentially life-threatening causes, such as increased intracranial pressure resulting in papilledema, should be considered (e.g., neuroimaging, typically contrast cranial MRI, and MRV followed by consideration for a lumbar puncture).

The fundoscopic exam of DP may also mirror NAION but sometimes shows a more distinctive disc with prominent telangiectasias and dilated vasculature of the optic disc. The optic disc edema in DP may be unilateral or bilateral, and diabetic macular edema (DME) is frequently a comorbid finding, occurring in up to 70% of patients. The presence of DME may be another differentiating ophthalmoscopic sign of DP compared with NAION. Other diabetic retinopathy (DR) findings, usually nonproliferative DR (NPDR), occur in the involved or unaffected eye in 35–90% of patients. An exam of the fellow eye typically shows a small optic disc cup (the structural disc at risk). The optic disc findings in DP typically resolve spontaneously in follow-up examinations, with a reported mean duration of 4–8 months (longer than typical NAION). Fluorescein angiography often shows disc leakage in patients with DP and also can better illustrate the radial pattern of dilated telangiectatic vessels that may help to differentiate DP from proliferative diabetic neovascularization of the disc (NVD) from NAION.

Differential Diagnosis

DP is considered a diagnosis of exclusion. The differential diagnosis includes papilledema, optic disc neovascularization, malignant hypertension, papillitis, and NAION.

Therapy

Although corticosteroids have been proposed in NAION, this is controversial in patients with DP because of the potential for worsening diabetic glucose control. Additionally, reports of intravitreal injection of vascular endothelial growth factor inhibitors (anti-VEGF), bevacizumab, and ranibizumab have been documented to show improvement of optic disc swelling and improved vision in anecdotal reports. However, several of these patients also had macular edema and larger studies are needed to accurately assess the efficacy of this therapeutic approach.

Prognosis

DP generally has a favorable prognosis with no required treatment beyond treating the diabetes, but it is essential to differentiate it from more malignant or aggressive processes including NAION, papilledema and other infectious and inflammatory papillitis.

Epidemiology

DP is a relatively uncommon condition considering the prevalence of diabetes mellitus. The estimated incidence of DP is 0.5%. Though it was initially described only in younger patients with type 1 diabetes, it has subsequently been documented in older type 2 diabetic patients (up to 79 years old). Though duration of diabetes is not an established risk factor, most cases of DP have been reported in patients with long-standing diabetes.

Cross-References

▶ Diabetic Disc Edema
▶ Nonarteritic Anterior Ischemic Optic Neuropathy

Further Reading

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Diabetic Retinopathy

▶ Early Treatment Diabetic Retinopathy Study (ETDRS)

Diabetic Retinopathy, Proliferative

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Synonyms

Proliferative retinopathy due to diabetes

Definition

Introduction and Definition

Proliferative diabetic retinopathy (PDR) is an advanced form of diabetic retinopathy characterized by the growth of new vessels arising from the optic disc, surface of the retina, iris, or anterior chamber angle. It is associated with a significant loss of vision and at least 12% of the new cases of blindness each year in the United States (Albert et al. 2008). Growth of new vessels at the disc is known as neovascularization of the disc (NVD), whereas origin of new vessels from retinal vasculature elsewhere is neovascularization elsewhere (NVE). As the disease progresses, fibrous tissue around the vessels increases, and when this fibrous tissue contracts, it can lead to tractional retinal detachment and vitreous hemorrhage, which are the leading causes of visual loss associated with PDR (Yanoff and Duker 2014).

The prevalence of diabetic eye disease is steadily increasing. More than 150 million people around the world suffer from diabetes, and this number is expected to double by the year 2030. In the background of this diabetes *tsunami*, diabetic retinopathy and its complications remain a major medical and social challenge.

Classification of PDR

Based on the clinical manifestations, diabetic retinopathy has been classified as either nonproliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR). PDR is marked by the presence of retinal neovascularization (Table 1).

Eyes with early PDR have a 75% risk of progression to high-risk PDR in a 5-year period. These eyes require prompt therapy with laser photocoagulation (Albert et al. 2008; Ryan et al. 2013).

Diabetic Retinopathy, Proliferative, Table 1 Classification of proliferative diabetic retinopathy (PDR)

Proliferative diabetic retinopathy (PDR) is characterized by NVD or NVE, preretinal or vitreous hemorrhage or fibrous tissue proliferation	
Early PDR	New vessels, but criteria for high risk not met
High-risk PDR	1. NVD (1/3–1/2 disc area)
	2. NVD and vitreous or preretinal hemorrhage
	3. NVE $\geq$1/2 disc area and vitreous or preretinal hemorrhage

Etiology

Systemic Risk Factors for Progression to PDR

(a) Glycemic control

In the majority of studies, poor glycemic control has been associated with an increase in the severity of diabetic retinopathy. Both the duration and severity of diabetes mellitus are known to affect the outcome in patients with retinopathy. The duration of diabetes has been directly associated with increased prevalence of retinopathy in the population with both type 1 and 2 diabetes. In patients with poor metabolic control, intensive therapy and achievement of good control of blood glucose have been shown to have an initial detrimental effect on the retina. However, after 3 years, intensive therapy has been shown to ultimately reduce the risk of progression of retinopathy in insulin-dependent diabetics (Albert et al. 2008).

(b) Systemic hypertension

The effect of hypertension on diabetic retinopathy is unclear. However, several studies have indicated that increased diastolic and systolic blood pressures may be associated with increased severity of progression of diabetic retinopathy (Albert et al. 2008).

(c) Nephropathy

In diabetic patients, it has been noted that the presence of diabetic nephropathy and increased urinary protein leakage is associated with an increased severity of diabetic retinopathy. Changes in the retina due to uremia include edema of the optic disc and the retina (Albert et al. 2008).

(d) Pregnancy

Pregnancy may result in an increased risk of progression of diabetic retinopathy attributed to physiological changes experienced during gestation. However, this difference may be small (Albert et al. 2008).

Ocular Risk Factors

Ocular risk factors that may result in progression to proliferative retinopathy in diabetes include cataract surgery, especially when complicated by rupture of the posterior capsule or vitreous loss. This may predispose the patient to higher levels of inflammation and the release of pro-inflammatory and angiogenic cytokines. Other various intraocular procedures are known to increase the risk of progression to PDR, including glaucoma surgery (Albert et al. 2008; Ryan et al. 2013).

Pathogenetic Role of Various Pro- and Anti-inflammatory Factors

The hallmark of diabetic retinopathy is microvascular damage due to tissue ischemia. This results in the release of various angiogenic factors that are thought to play a role in the development of PDR. Among these factors, vascular endothelial growth factor (VEGF) is thought to play the most important role, as indicated by the high concentration of VEGF in the vitreous of eyes with PDR. Additionally, the angiogenic properties of the vitreous fluid from eyes with PDR can be blocked with the addition of a VEGF inhibitor in vitro. Along with VEGF, it is thought that angiopoietin, erythropoietin, basic fibroblast growth factor, insulin-like growth factor, protein kinase C, tumor growth factor, interleukins (IL-1, IL-6, and IL-8), and platelet-derived growth factor also play a role in the pathogenesis of PDR (Ryan et al. 2013; Yanoff and Duker 2014).

Neovascularization occurs in response to these factors in the retina and other ocular structures. New vessels start out small, but they typically progress to a caliber that is one eighth to one fourth the size of a major retinal vein found at the optic disc margin (Ryan et al. 2013).

Pathogenesis of Fibrous Proliferation and Retinal Traction

Retinal neovascularization is accompanied by a proliferation of white fibrous tissue adjacent to the vessels. These neovascular networks found on the retina nearly always form adhesions with the vitreous. Over time, the fibrous tissue along the posterior vitreous contracts, and as it does so, it causes a forward force on the posterior vitreous that results in its detachment from the retinal surface. However, the vitreous remains attached to the retina at the points of adhesion formed with the new vessels. Vitreous traction on these vessels results in vitreous hemorrhage, which is one of the main causes of visual loss associated with PDR. Vitreous hemorrhage results in pooling of blood in the posterior fluid vitreous, and it typically requires many months for the blood from a large hemorrhage to be absorbed. When a large sheet of fibrovascular tissue contracts, it may also result in a displacement of the macula, typically nasally and somewhat vertically toward the optic disc as this is a common site of neovascularization. Vitreoretinal adhesions also present the risk of tractional retinal detachment (TRD) following the contraction of the areas of fibrovascular proliferation. TRD may be relatively minor or it may be a more extensive detachment (Ryan et al. 2013).

The development of PDR is illustrated in Fig. 1.

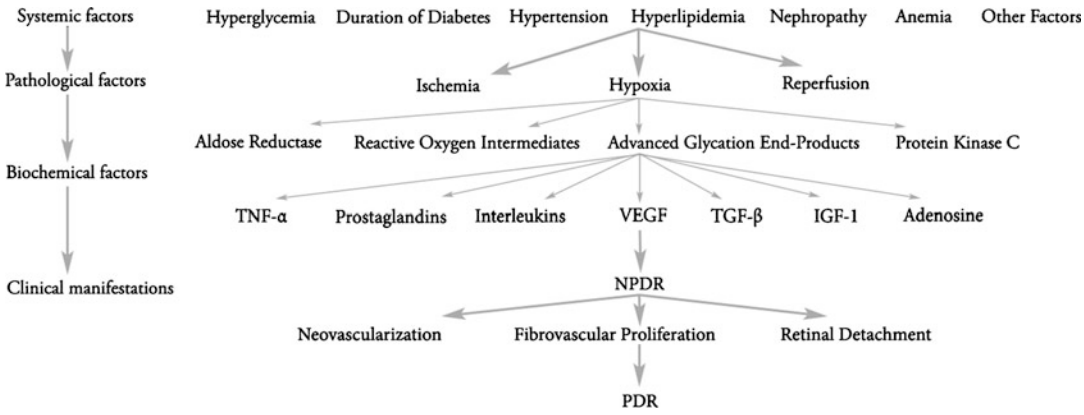
Clinical Presentation

Visual Acuity

Patients with PDR are at an increased risk of blindness due to various complications including vitreous hemorrhage, TRD, and macular edema. Severe visual loss (SVL), defined as 5/200 or worse on two consecutive visits 4 months apart, can be reduced substantially by early treatment in patients with PDR. The 5-year risk of SVL in patients with PDR is as high as 60% if left untreated (Albert et al. 2008).

Symptomatology

Patients with PDR present with decreasing vision due to various causes including macular edema. There may be a sudden drop in vision or floaters in patients secondary to vitreous hemorrhage or retinal detachment. PDR results in blindness in a majority of patients due to unresolved vitreous hemorrhage (Ryan et al. 2013).



Diabetic Retinopathy, Proliferative, Fig. 1 Flowchart showing the risk factors for development of proliferative diabetic retinopathy. The chart summarizes the systemic, biochemical, and local factors responsible for the clinical manifestations of proliferative diabetic retinopathy. *IGF* Insulin-like growth factor, *NPDR* nonproliferative diabetic retinopathy, *PDR* proliferative diabetic retinopathy, *TGF* transforming growth factor, *TNF* tumor necrosis factor, *VEGF* vascular endothelial growth factor

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Other Measures of Visual Function

PDR may also affect a number of other visual functions including visual fields. Retinal detachment secondary to traction may result in scotomas. Treatment including laser photocoagulation is associated with peripheral field constriction. Electroretinogram (ERG) shows evidence of decreased function of photoreceptors. Vascular manifestations of the retina may be associated with changes in the b-wave of the ERG. ERG may also be used to predict the prognosis after surgery in eyes with dense vitreous hemorrhage (Ryan et al. 2013).

Anterior Segment Features

Slit lamp biomicroscopy in patients with PDR may reveal the presence of floating red blood cells in the anterior chamber in patients with vitreous hemorrhage. There may be increased progression of nuclear sclerosis resulting in media opacity and decreased vision. Iris neovascularization (INV) may result due to the effect of VEGF in the anterior chamber. On gonioscopy, small tufts of anterior chamber angle new vessels (ANV) may be evident in certain patients. Patients with NPDR may progress to PDR after complicated cataract surgery with signs of posterior capsular rupture. Examination of the vitreous may show presence of deep red glow or red blood cells floating in patients with vitreous hemorrhage (Skuta et al. 2011; Ryan et al. 2013).

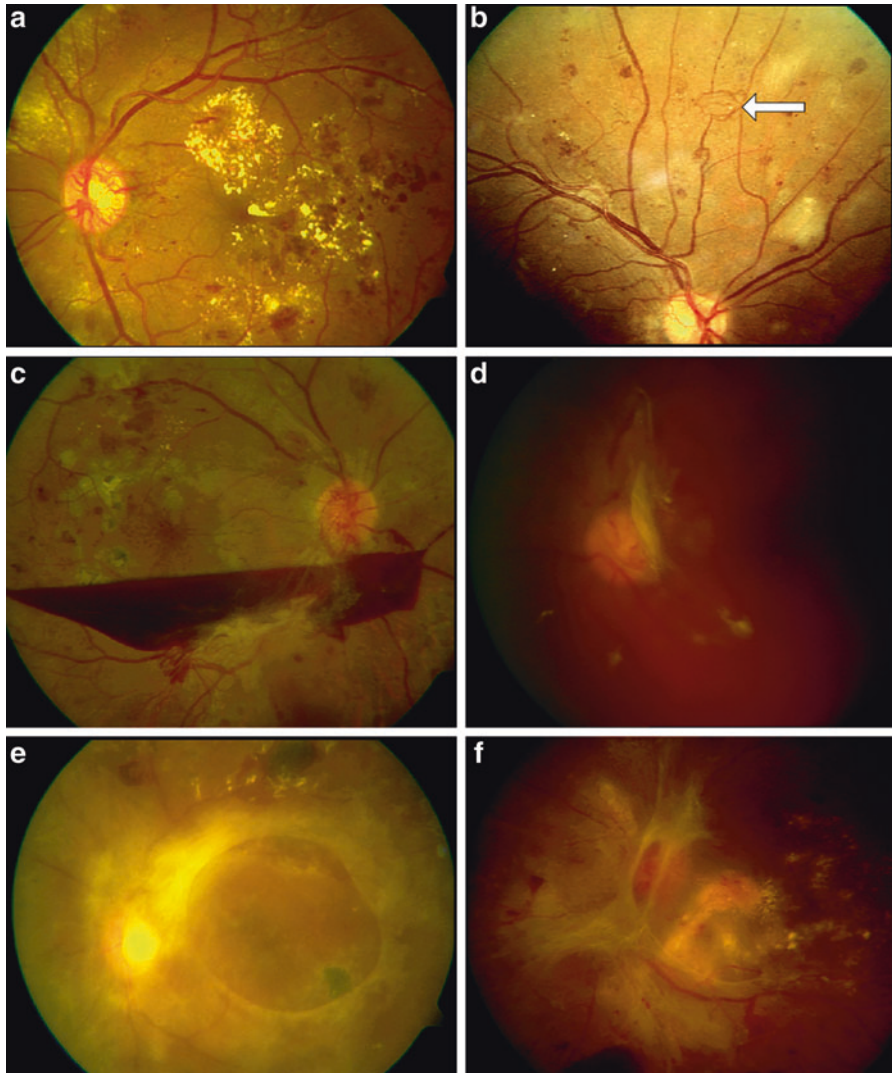
Posterior Segment Features

(a) Diabetic retinopathy

Background diabetic retinopathy consists of changes in the retinal microvasculature including microaneurysms, dilation and beading of the retinal venules, thinning of the retinal arterioles, intraretinal microvascular abnormalities, nerve fiber layer infarcts (cotton wool spots), retinal edema, intraretinal hemorrhages, and hard exudates that appear as discrete, yellow intraretinal deposits composed of lipids (Skuta et al. 2011; Ryan et al. 2013).

(b) Retinal neovascularization

New retinal vessels may be present anywhere on the retina, but they are most frequently seen in the posterior pole. They may present as neovascularization of the disc (NVD; Fig. 2a) or as neovascularization elsewhere (NVE; Fig. 2b). The newly formed vessels often take the form of a wheel, with the vessels radiating outward from a central complex like the spokes of a wheel and joining with a vessel surrounding the circumference of the neovascular network. However,



Diabetic Retinopathy, Proliferative, Fig. 2 Fundoscopic features of proliferative diabetic retinopathy (*PDR*). (**a**) Neovascularization of the optic disc (NVD) appears as a fine, lacy pattern of new vessels on the optic nerve head. (**b**) Neovascularization elsewhere (NVE) (marked with a *white arrow*) more than half the size of optic disc in a patient with high-risk characteristics PDR. (**c**) Subhyaloid hemorrhage appears as a typical boat-shaped, dark-colored collection of blood behind the posterior hyaloid membrane. (**d**) Vitreous hemorrhage resulting in obscuration of media clarity is a major cause of poor vision in patients with PDR. (**e**) Tractional retinal detachment is seen in a patient with advanced PDR forming a tabletop configuration at the macula. (**f**) Combined retinal detachment results due to the development of a large retinal break in a patient with tractional retinal detachment, requiring surgical intervention

they may also assume an irregular shape (Ryan et al. 2013). The irregular vessels can be distinguished from normal vessels because they cross both arterioles and venules (Albert et al. 2008; Yanoff et al. and Duker 2014).

(c) Vitreous/preretinal hemorrhage

Complete detachment of the posterior vitreous occurs naturally with aging in diabetic patients. However, among patients with PDR, neovascular proliferations remain attached to

the posterior vitreous, major retinal vessels, and the optic disc. Traction on these adhesions can result in vitreous or preretinal hemorrhage. When the blood is limited by the posterior hyaloid, it is termed a preretinal hemorrhage or subhyaloid hemorrhage (Fig. 2c). The break in the continuity of the posterior hyaloid phase results in vitreous hemorrhage (Fig. 2d) (Albert et al. 2008).

(d) Fibrous proliferation/tractional retinal detachment (TRD)

Contraction of fibroproliferative tissue may be associated with TRD (Fig. 2e). On indirect ophthalmoscopy, the retina appears pulled and concave in configuration with limited mobility. The traction may progress resulting in the formation of a tabletop configuration of the TRD (Ryan et al. 2013).

(e) Combined retinal detachment

Pulling and traction on the retina may result in the development of subsequent retinal breaks and seepage of fluid underneath the retina, resulting in a combined retinal detachment (Fig. 2f). The detached retina assumes a convex configuration and corrugations with underlying subretinal fluid (Ryan et al. 2013).

Macular Edema in PDR

As the severity of diabetic retinopathy progresses, there is an increased risk for the development of diabetic macular edema (DME). Edema occurs due to the incompetence of the retinal capillaries and subsequent exudation leading to retinal thickening. If the edema occurs in the macula, this poses a significant threat to vision. The presence of hard exudates in the foveal center may have detrimental effects on vision (Albert et al. 2008).

Neovascular Glaucoma

Neovascular glaucoma occurs when proliferation of new vessels occurs in the anterior chamber angle, leading to an obstruction in aqueous outflow and a subsequent rise in intraocular pressure. It is thought to occur due to the diffusion of pro-angiogenic factors from the ischemic retina. Eyes with neovascular glaucoma may have a poor visual outcome (Ryan et al. 2013).

Involutional PDR

In the end stage of the disease, diabetic retinopathy becomes involutional or quiescent. This occurs after vitreous contraction is complete and the vitreous remains attached to the retina only at locations where there are adhesions with new vessels. At this stage, there is a decrease in vitreous hemorrhage, and retinal vessels typically return to their previous size or smaller. The visual outcome in this stage is variable. Loss of vision in this stage is related to macular ischemia, edema, and detachment, as well as opacity within the globe or optic nerve disease (Ryan et al. 2013).

Diagnosis

Schedule for Screening for PDR

Patients diagnosed with both non-high-risk and high-risk PDR should be examined every 2–3 months with careful follow-up to identify progression or potential complications (Skuta et al. 2011).

Clinical Examination

Diagnosis of PDR is established clinically using slit lamp biomicroscopy and indirect ophthalmoscopy. Examination of the periphery may reveal the presence of retinal microvasculature abnormalities including neovascularization (Yanoff and Duker 2014).

Fluorescein Angiography

Fluorescein angiography of the retina is used for both the diagnosis and management of diabetic retinopathy. Standard 7-field photography is performed to identify various changes in microvasculature including telangiectasias, microaneurysms, and leakage from new blood vessels (NVD or NVE). There may be accumulation of dye resulting in hyperfluorescence at the posterior pole due to macular edema. Patients with PDR may present with an irregular foveal avascular zone (FAZ) and extensive areas of retinal capillary non-perfusion (CNP).

Wide-field photography performed using newer technology can provide a wide-field view

of the fundus and can help identify various retinal pathologies that begin in the periphery. Significant microvascular changes in the retina of patients with diabetic retinopathy identified by fluorescein angiogram may predict the risk of progression to PDR (Skuta et al. 2011; Ryan et al. 2013).

Optical Coherence Tomography (OCT)

Optical coherence tomography (OCT) imaging is a very important tool in monitoring status of disease in patients with PDR. There may be diffuse thickening, distortion, and other irregularities within the retina due to contraction of the fibrovascular tissue. If DME is present, fluid will be seen within the macula along with retinal thickening. Abnormalities may be found at the vitreoretinal interface due to vitreoretinal adhesions. These may be associated with TRD, which can be visualized as an accumulation of fluid beneath the retina. OCT is of particular value in cases of TRD because it allows for an assessment of macular and foveal involvement and thus may aid in determining subsequent plans for treatment (Ryan et al. 2013).

Differential Diagnosis

Hypertensive Retinopathy

With a chronic elevation in blood pressure, the blood-retina barrier becomes disrupted, leading to an exudative phase in which microaneurysms, retinal hemorrhages, hard exudates, and cotton wool spots may be found in the retina, leading to similar findings to those of diabetic retinopathy (Ryan et al. 2013; Yanoff and Duker 2014).

Retinal Vasculitis

Retinal vasculitis may present with microvascular abnormalities including exudation, sheathing, and retinal neovascularization. These findings may be similar to changes found in PDR. However, unlike PDR, retinal vasculitis may be associated with signs of ocular inflammation (Albert et al. 2008).

Hemoglobinopathies

The hemoglobinopathies result from a number of mutations in the hemoglobin subunits, with the most common form being sickle cell disease (SCD). Similar to PDR, eyes of patients with SCD may show neovascularization of the retina due to tissue ischemia, which may lead to vitreous hemorrhage and vision loss (Ryan et al. 2013).

Miscellaneous

Various retinal pathologies may mimic PDR, including retinal macroaneurysms, retinal vein occlusions, and ocular ischemic syndrome, to name a few (Ryan et al. 2013).

Therapy

Panretinal Photocoagulation (PRP)

i. Indications

Panretinal photocoagulation (PRP) is an important treatment modality for patients with PDR. High-risk PDR is an indication for PRP, and the disease usually has a poor outcome without treatment.

Additional indications include INV, ANV, moderate to severe NVE without vitreous or preretinal hemorrhage, and the presence of widespread capillary dropout and retinal ischemia as demonstrated by fluorescein angiography. PRP may be performed in patients unlikely to follow-up. Special consideration may also be given to pregnant women with PDR and to the second eye of a juvenile diabetic when the other eye has severe PDR (Albert et al. 2008).

ii. Technique

PRP may be done with multiple wavelengths and instruments, but a 514 nm argon green laser is most commonly used. For adults, a transpupillary slit lamp approach is most common. Topical anesthesia is typically sufficient. The duration of each laser pulse is typically 0.1–0.2 s, and each pulse creates a burn that is about 500 μm in diameter. The laser is typically placed one-half burn width

apart. Treatment is given panretinally, typically over a series of two to three sessions. A total of 800–1,600 burns are created with avoidance of the macula and optic disc. Additional laser therapy may be required if there is persistence of neovascularization. One must avoid areas of fibrous tissue proliferation and vitreoretinal traction during laser (Albert et al. 2008).

iii. Results

The Diabetic Retinopathy Study (DRS) was a large-scale study intended to assess the benefits of laser photocoagulation in patients with diabetes mellitus. According to the DRS, eyes with PDR and high-risk characteristics have a 25% risk of developing severe visual loss within 2 years. However, treatment with PRP is able to reduce this risk by 50% (Albert et al. 2008; Yanoff and Duker 2014).

One of the objectives of the Early Treatment of Diabetic Retinopathy Study (ETDRS) was to determine the optimal timing of laser photocoagulation in eyes with diabetic retinopathy. The data showed that, for patients with type II diabetes, there is a benefit in early treatment with PRP of eyes with severe NPDR or early PDR. These recommendations, however, must be taken into consideration along with other factors such as health of the other eye and other clinical findings (Albert et al. 2008).

iv. Complications

Treatment with PRP has been demonstrated to protect against severe visual loss in eyes with PDR, but complications may still arise. There may be pain during treatment and intraocular pressure may transiently elevate. There may be temporary loss of accommodation, decreased night vision, color vision, glare, and photopsia. More severe complications that may occur include foveal burns, optic disc damage, macular edema, hemorrhages, retinal detachment, corneal abrasions, lens opacities, and loss of visual field (Albert et al. 2008).

Vitrectomy for PDR

i. Indications

There are many indications for pars plana vitrectomy (PPV) in eyes with PDR. PPV may be indicated in the presence of non-clearing dense vitreous hemorrhage or subhyaloid and premacular bleeds. PPV is also indicated in eyes with TRD that involves the macula and combined retinal detachment. PPV may be performed in diffuse macular edema with a taut posterior hyaloid membrane. Additional indications include red blood cell induced glaucoma and anterior hyaloid proliferation. In eyes with iris neovascularization and lens opacities, PPV is indicated so that an endolaser may be used for PRP treatment of the retina. With advancements in surgical techniques, the indications of PPV have expanded to include many clinical scenarios (Albert et al. 2008; Ryan et al. 2013).

ii. Technique

The main goals of vitrectomy are to remove media opacities such as hemorrhage and to relieve vitreous traction on the retina that is resulting in detachment, distortion, or displacement of the fovea (Albert et al. 2008). The most commonly used technique is PPV with three port entry sites. With recent advances in surgical instrumentation, PPV is increasingly being performed using smaller gauge vitrectomy systems including 23- and 25-gauge techniques instead of conventional 20-gauge systems. Higher cut rates and aspiration parameters are now available to ensure better surgeon control. Specialized instrumentation may be required to aid in surgeon manipulation, including intraocular scissors to cut the fibrous tissue, intraocular pick and forceps, chandelier illumination system, and bimanual cautery. PRP with the use of an endolaser is performed during a vitrectomy in eyes with PDR in order to ensure treatment of areas in the retinal periphery and around areas of neovascularization. In complicated cases of retinal detachments, additional agents may be used for surgical ease. These include

the use of intraoperative heavy perfluorocarbon liquid in patients with complex retinal folds. Filtered air may then serve as a short-term tamponade, and gases such as SF_6, C_2F_6, and C_3F_8 may provide longer tamponade for 2–8 weeks. Silicone oil can be used as a tamponade in cases requiring a longer tamponade such as reoperations or severe cases (Ryan et al. 2013).

iii. Results

Results following vitrectomy vary depending upon the indication for the surgery. In eyes with vitreous hemorrhage only, about three quarters of patients will have improvements in vision 6 months after surgery and the similar number will have a visual acuity of 5/200 or better. In eyes with TRD that involves the fovea, about one half to three quarters will have improvements in visual acuity and about half will have a visual acuity of 20/200 or better at 6 months. However, less than a quarter of these patients may experience recurrent macular detachment. About two thirds of eyes with combined detachment attain long-term macular reattachment post vitrectomy and improved visual acuity is seen in about half of the cases (Albert et al. 2008).

iv. Complications

Cataracts may form postoperatively due to inadvertent intraoperative lens touch or due to exposure to the tamponade gas postoperatively. Injury to the cornea may also occur during the time of surgery. Hemorrhage may occur postoperatively but usually clears spontaneously over several weeks. If the hemorrhage is so extensive that the fundus cannot be visualized, ultrasound is recommended to rule out retinal detachment (Ryan et al. 2013). Ghost cell glaucoma and endophthalmitis are rare, but serious, complications of vitrectomy. INV and ANV may also occur postoperatively in cases where retinal ischemia is not adequately treated with endolaser (Albert et al. 2008).

v. Advances: transconjunctival sutureless vitrectomy (TVS)

With recent advances in technology, vitrectomy may now often be performed using 23- or 25-gauge trocars and small gauge vitrectomy instruments. The small incisions necessary for this technique are self-sealing and rarely require sutures and may lead to shorter times in the operating room, faster visual recovery, and improved patient comfort postoperatively. However, they also have disadvantages of increased postoperative retinal tears, endophthalmitis, and hypotony (Skuta et al. 2011).

Pharmacologic Vitreolysis

In diabetic eyes, it has been observed that complete posterior vitreous detachment is associated with a decreased risk of developing PDR. While this may be achieved through vitrectomy, pharmacologic vitreolysis may provide a less invasive means of achieving a posterior vitreous detachment. Various agents including plasmin, tissue plasminogen activator, microplasmin, and hyaluronidase have been investigated as potential vitreolytic agents. Future research may show pharmacologic vitreolysis to be an effective means of achieving posterior vitreous detachment and delaying the onset of PDR (Ryan et al. 2013).

Role of Intravitreal Anti-VEGF Injections

VEGF inhibitors such as bevacizumab and ranibizumab have been demonstrated to counteract the neovascular complications of PDR. The effects of these agents appear to be temporary and require repeated dosing. However, there is some evidence to indicate that, after a period of treatment with these agents, reduction in the frequency of the dosing may be possible without reactivation of the disease (Ryan et al. 2013). Anti-VEGF injections have shown to reduce the chances of development of PDR by various studies including RISE and RIDE. Presently, the use of anti-VEGF therapy for PDR is continuously evolving (Yanoff and Duker 2014).

Other Surgical Modalities

(a) Anterior retinal cryopexy (ARC)

The use of cryotherapy to cause aseptic chorioretinal inflammation in the anterior

retina has been performed in certain patients with PDR and vitreous hemorrhage. Ablation of peripheral retina with ARC is performed with an aim to destroy the ischemic retina. Peripheral cryopexy must be avoided in patients with known TRD. ARC is no longer a preferred modality due to its higher number of complications (Ryan et al. 2013; Yanoff and Duker 2014).

(b) Pituitary ablation

In the past, suppression of the pituitary gland was used as a means to control the vascular changes seen in PDR. Methods included external irradiation, transfrontal hypophysectomy, and transsphenoidal implantation of yttrium. The benefits seen in pituitary ablation are thought to stem from the suppression of growth hormone and its effects on insulin-like growth factor. Pituitary ablation as a means to control PDR is of little significance due to other methods such as photocoagulation being more effective while avoiding the side effects of a hypopituitary state (Ryan et al. 2013).

Prognosis

Eyes with PDR are at a significant risk for visual loss. Among eyes with PDR, those with one or more high-risk characteristics are at a greater risk for visual loss. The most common causes of visual loss in PDR are vitreous hemorrhage and traction retinal detachment. Visual loss may also occur due to distortion or displacement of the macula, macular edema, and neovascular glaucoma (Ryan et al. 2013).

Epidemiology

The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) was a population-based study that provided information regarding the epidemiology of diabetic retinopathy. According to the study, 23% of patients with type I diabetes and 6% with type II diabetes had PDR. In addition, the risk of progression to PDR among type I diabetics was 10.5% over a 4-year period. This risk was 7.4% and 2.3% for type II diabetics taking and not taking insulin, respectively (Ryan et al. 2013). It has been reported that after the diagnosis of type 2 diabetes, 67% of patients develop retinopathy and 10% have PDR (Yanoff and Duker 2014).

According to the available data, diabetic retinopathy was more prevalent in type II diabetic African Americans when compared to whites but similar in type I diabetics. Mexican Americans with both type I and type II diabetes have been shown to have higher frequencies of diabetic retinopathy when compared to non-Hispanic whites. Initial data on Native American diabetics indicated higher frequencies of diabetic retinopathy when compared to whites, but more recent data indicates that it likely varies between different Native American groups. Among Chinese Americans, the incidence of retinopathy was similar when compared to whites, but they showed higher rates of progression to more severe forms of the disease (Ryan et al. 2013).

Cross-References

- Angiography, Fluorescein
- Antivascular Endothelial Growth Factor
- Blood-Retina Barrier
- Diabetic Macular Edema
- Diabetic Retinopathy
- Early Treatment Diabetic Retinopathy Study (ETDRS)
- Neovascularization, Retinal
- Pars Plana Vitrectomy
- Posterior Vitreous Detachment
- Retinal Detachment

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Diamox

► Acetazolamide for Pseudotumor Cerebri

Diathermy

► Thermal Cautery

Dichromatic Vision

► Achromatopsia Cerebral

Diffractive Intraocular Lens

► Apodized Diffractive Intraocular Lens

Diffuse Retinal Pigment Epitheliopathy

► Central Serous Chorioretinopathy/ Choroidopathy

Diffusion-Weighted Magnetic Resonance Imaging

► Diffusion-Weighted MR Image

Diffusion-Weighted MR Image

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Synonyms

Diffusion-weighted magnetic resonance imaging; DWI

Definition

Diffusion-weighted imaging (DWI) is a well-established magnetic resonance imaging (MRI) sequence that is dependent upon random "Brownian motion" of water molecules. DWI was first introduced to clinical practice in the 1990s and has been applied to the evaluation of various intracranial diseases. DWI has shown the capability in detecting early and subtle changes within the brain prior to any visible abnormality can be detected on the conventional imaging. DWI has shown superb sensitivity in the detection of acute brain ischemia and in the differentiation of acute infarction from other intracranial disease processes. The reported sensitivity ranges from 88% to 100% and specificity from 86% to 100%. Restricted diffusion in ischemic brain tissue can be observed within few minutes after acute brain ischemia, while conventional (T1/T2) MRI

sequences may not demonstrate the infarct until 6 h or more and may be especially hard to appreciate on CT even after several hours to days.

Basic Characteristics

Physics

To obtain DW images, a pair of strong gradient pulses is added to the pulse sequence to dephase and rephase the spins if no net movement occurs. If net movement occurs, this leads to signal attenuation. The degree of signal reduction depends on the extent of molecular translation and diffusion weighting. The extent of diffusion weighting is determined by the strength of the diffusion gradients, the time between the gradient pulses, and the duration of the gradients.

The diffusion data can be presented as signal intensity or an image map of the apparent diffusion coefficient (ADC). ADC calculation requires two or more acquisitions with different diffusion weightings. Low ADC corresponds to high signal intensity (restricted diffusion), and a high ADC corresponds to low signal intensity on DWI. The degree of restriction of water diffusion in biologic tissue is inversely correlated to the tissue cellularity and the integrity of cell membranes.

In acute brain ischemia, if the cerebral blood flow drops to 10 ml/100 g/min, the cell membrane ion pumps will fail, and the excess sodium will enter the cell, this will cause movement of water from the extracellular to intracellular compartment and cytotoxic edema. The diffusion of the intracellular water molecules is restricted by the cell membranes. Thus, the restricted diffusion of water causes a decreased ADC and increased signal intensity on DWI. This restricted diffusion appears as bright on DWI and dark on ADC.

Clinical Application

The clinical applications of DWI are increasingly widespread. The major clinical applications for DWI are as follows:

- To diagnose acute ischemic stroke
- To differentiate stroke from stroke mimics
- To differentiate epidermoid cyst from arachnoid cyst
- To differentiate brain abscess from necrotic tumors
- To assess cortical lesions in Creutzfeldt Jakob disease (CJD)
- To differentiate herpes encephalitis from diffuse temporal gliomas
- To assess the extent of diffuse axonal injury
- To assess active multiple sclerosis plaques

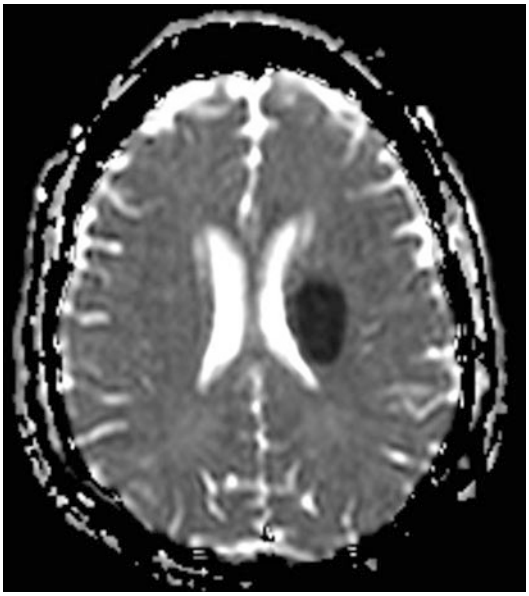
D

Radiographic Features

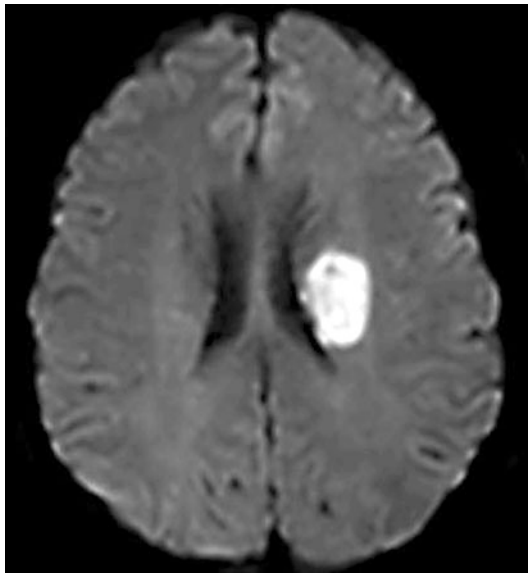
The time line of the radiographic features of DWI/ADC in acute brain ischemia is as follows:

Acute (0–7 days):

- Marked hyperintensity on DWI and hypointensity on ADC images.
- Maximal signal reduction of ADC is 1–4 days.



Diffusion-Weighted MR Image, Fig. 1 Apparent diffusion coefficient (ADC) sequence of MRI shows a hypointense lesion that corresponds to the hyperintense lesion on diffusion weighted imaging (DWI)



Diffusion-Weighted MR Image, Fig. 2 This combination of hypointensity on ADC and hyperintensity on DWI is consistent with restricted diffusion (e.g., acute ischemic stroke)

- Cytotoxic and vasogenic edema and extravasation of water molecules from blood vessels due to the release of inflammatory mediators from ischemic brain tissue.

Subacute (1–3 weeks):

- (7–15 days) ADC pseudonormalization.
- ADC rise and return to near baseline.
- Permanent tissue necrosis despite normalization of ADC.
- DWI hyperintensity due to T2 shine through (ADC and DWI bright).
- After 2 weeks ADC rises and becomes hyperintense.

Chronic (>3 weeks):

- ADC hyperintensity
- DWI hypointensity (T2 hyperintensity and T2 shine through resolve) (Figs. 1 and 2)

Cross-References

► Diffusion-Weighted Magnetic Resonance Imaging

Further Reading

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Dimple Wart

► Molluscum Contagiosum: Overview

Diode Lasers

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Definition

As the name suggests, the active medium in a diode laser is a semiconductor diode. These lasers are mostly pumped electrically by applying voltage across the diode. The electron and holes from the two-doped sides of the diode recombine on the application of voltage leading to the generation of light.

Principle of Operation

Diode lasers use p-i-n diode, where p-region is a positively doped semiconductor having excess positively charged entities (holes), n is a

negatively doped semiconductor having excess negatively charged entities (electrons), while i is the intrinsic layer which is uncharged. When a voltage is applied across the p-i-n diode, the positive voltage drives the holes from the p-region toward the n-region, while the negative voltage on the n-region drives the electrons toward the p-region (Fig. 1). The electrons and holes recombine in the i-region resulting in the generation of light. This electron hole recombination in itself does not cause lasing. However when the diode is kept inside a cavity, population inversion happens for a wavelength, which belongs to one of the longitudinal modes of the cavity and lasing is observed. In diode lasers the cavity is a waveguide made on the semiconductor crystal. The light is confined in the waveguide, and the two ends of the crystal are cleaved and polished to act as reflectors (Fig. 1).

Material

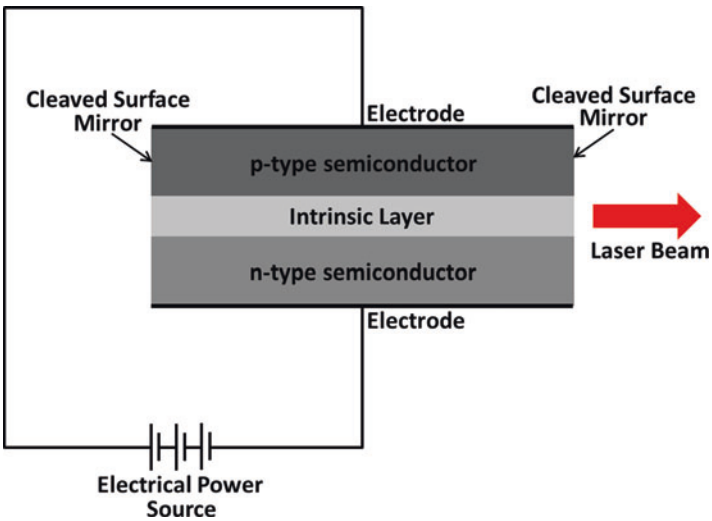
Diode lasers are fabricated using special semiconductor materials. Most of the naturally available semiconducting materials such as silicon and germanium have atomic orientation which does not allow the energy from the electron hole recombination to be emitted as light. Only those semiconductors where electron hole recombination results in the generation of a photon can be used in fabricating diode laser. III/V type semiconductors such as gallium arsenide or indium phosphide are suited for this purpose.

Beam Quality

The output beam from the laser diodes usually is elliptical with higher divergence in one axis as compared to the other. This is because the cavity for laser diodes is asymmetrical, wider in one direction and narrower in the other. Due to diffraction the beams come out more divergent along the axis, which is narrower and less divergent along the axis, which is wider. This elliptical orientation of the laser diode beam is usually corrected using cylindrical lens.

Output Power

Diode lasers can have output powers ranging from hundreds of microwatts to tens of kilowatts. The low output power laser diodes have good beam quality, which is obtained by making a narrow waveguide. To increase output power, laser diodes



Diode Lasers, Fig. 1 Schematic of the diode laser

with a wider waveguide are used. The output from multiple laser diodes is then combined together using additional optics to increase output power in the range of kilowatts.

Emission Wavelengths

The diode lasers' emission wavelength ranges from near UV to mid-IR with the shortest wavelength being 375 nm to the longest wavelength of 3,330 nm. The most common output wavelengths of emission are in 760–980 nm, 1,310 nm, and 1,550 nm.

Applications

Diode lasers are cheap and compact and provide high output power. This makes them ideal for various applications. They are extensively used in telecommunications as their output power can be easily modulated. They are also used in a variety of other equipments such as range finders, barcode readers, DVD players, laser pointers, etc. High-power diode lasers are used in industrial applications such as seam welding, heat treating, and brazing. High-power diode lasers are also used as pumping sources for solid-state lasers. Diode lasers have been so successful that they are now replacing other types in almost every area of application of lasers.

In the area of ophthalmology, diode lasers are being used in retinal photodynamic therapy where a light-sensitive medicine is injected into the bloodstream. Once the medicine reaches the macula, light from the diode laser is shined into the eye. The medicine is activated by the laser light and creates blood clots in the abnormal blood vessels. This slows the scar tissue growth in the retina, thus reducing the damage to the cells in the macula. Another similar application of diode laser is the retinal photocoagulation, where the heat generated from the laser shined into the retina and blocks the abnormal blood vessel.

Diode laser technology is still an active area of research where new techniques are being developed to achieve compact design, improved beam quality, and higher power with greater conversion efficiency. With these advances diode lasers are expected to be used for various new applications in different areas of science and technology, including ophthalmology.

Cross-References

▶ Age-Related Macular Degeneration

Diopter: Definition

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Synonyms

Dioptre

Definition

A diopter ([D] or [dpt]) is a unit of measurement of the optical power of a lens or curved mirror, which is equal to the reciprocal of the focal length measured in meters (unit is 1/m). For example, a 2 diopter lens focuses an object at infinity to an image plane at a distance of 0.5 m. The term was proposed by French ophthalmologist Ferdinand Monoyer in 1872 based on the term dioptrice by Johannes Kepler.

Dioptre

▶ Diopter: Definition

Diplopia in Graves' Ophthalmopathy

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Synonyms

Graves' orbitopathy; Thyroid associated orbitopathy (TAO); Thyroid eye disease (TED)

Definition

Graves' disease is an acquired autoimmune phenomenon with a genetic predisposition characterized by the production of thyroid-stimulating immunoglobulins (TSIs). TSIs are autoantibodies that mimic the function of thyroid-stimulating hormone (TSH) by binding to TSH receptors in the follicles of the thyroid. Once TSI is bound, the TSH receptor is activated and transmits nuclear signals to increase production and secretion of thyroid hormone leading to a hyperthyroid state. The TSIs also cause hyperplasia and hypertrophy of the follicular tissue leading to diffuse goiter clinically. It is the most common cause of hyperthyroidism in the developed world.

The adjusted annual incidence rate is 16 females and 3 males per 100,000 people. The most common associated ocular findings include a dry, gritty ocular sensation, excessive tearing, photophobia, diplopia, and a pressure sensation behind the eye. Although Graves' disease is a common cause of thyroid eye disease, autoimmune thyroid disease can present with hypothyroidism (e.g., Hashimoto's thyroiditis) or with antibodies (e.g., TPO or TSIg) but normal thyroid function (euthyroid Graves' orbitopathy).

Diplopia, or seeing double, occurs when thyroid antibodies bind to the fibroblasts in the extraocular muscles and produce secondary inflammation. This causes a conversion to adipocytes which build up in the muscles and cause inflammation. The inflammation then compresses veins, prevents drainage, and subsequently causes edema. Hence this diplopia is generally restrictive rather than paralytic. Inflammation and edema in the extraocular muscles cause gaze abnormalities as muscle function is directly affected. The inferior rectus muscle is the most commonly involved extraocular muscle, and therefore, diplopia is most often encountered upon lateral upgaze. Eye elevation can also be limited secondary to fibrosis of the muscle. The second most commonly affected muscle is the medial rectus; however, multiple muscles can be affected and are not necessarily disturbed symmetrically. Diplopia is usually intermittent but can become chronic. The most common order of involvement for extraocular muscles in thyroid eye disease includes the inferior rectus, medial rectus, superior rectus, and lateral rectus. Patching, prism wear, or strabismus surgery are reasonable symptomatic treatments.

While orbital radiotherapy has been shown to treat refractory diplopia, radiation comes with its own set of risks and should be evaluated on a case-by-case basis. For patients with increasing diplopia, attempting to suppress the immune system with a trial of oral corticosteroids can be initiated.

Cross-References

▶ Graves' Disease

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Diplopia in Multiple Sclerosis

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Synonyms

Demyelinating disease; MS

Definition

Multiple sclerosis (MS) is a chronic, inflammatory, autoimmune, demyelinating disease of the central nervous system (CNS). Patients with MS may present with or develop diplopia. One of the most common presentations is a lesion of the medial longitudinal fasciculus (MLF) known as an internuclear ophthalmoplegia (INO). An INO may be seen in up to 25% of patients with MS. This lesion affects the connection between the abducens nerve nucleus and the contralateral medial rectus subnucleus of the third cranial nerve. Adduction of the affected side is impaired on horizontal gaze, and there is typically a dissociated horizontal abducting nystagmus in the fellow eye. Convergence may be spared if the near pathway located more rostrally is intact. Bilateral INO is often due to MS and patients may develop a concomitant exotropia with either monocular or binocular INO. Patients with MS can also have demyelinating pontine lesions that involve the abducens nucleus and MLF (i.e., the one-and-a-half syndrome). Involvement of the sixth nerve fascicle in the pons might also produce binocular horizontal diplopia in MS. Other isolated cranial nerve palsies of the third and fourth nerves however are less common in MS. Brain stem lesions may also produce skew deviation and binocular vertical diplopia.

Cross-References

▶ Internuclear Ophthalmoplegia
▶ One-and-a-Half Syndrome

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Diplopia in Myopathies

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Definition

Several systemic myopathies cause ocular motility disorders but most do not. Most myopathies are systemic or genetic diseases, and the motility problems are bilateral, insidious in the onset, and symmetric. Therefore, diplopia is rarely a presenting complaint as it usually requires an asymmetric lesion. These disorders include various forms of chronic progressive external ophthalmoplegia (CPEO). Four myopathies are specifically known to cause ocular motility disorders from a young age: Kearns-Sayre syndrome, oculopharyngeal muscular dystrophy, myotonic dystrophy, and myotubular myopathy. Kearns-Sayre syndrome is a mitochondrial myopathy in which the ophthalmoplegia appears between the ages of 5 and 20. Oculopharyngeal muscular dystrophy is an autosomal dominant disease that mainly affects patients with a French-Canadian descent and presents around the age of 40. Ptosis is generally a more common feature of this disorder. Myotonic dystrophy is a trinucleotide (CTG) repeat disorder. While the congenital form is more severe, the classic form begins in adolescence or adulthood with eccentric gaze holding difficulty, slow saccades, and ptosis. Finally, myotubular myopathy is an X-linked disorder in which patients exhibit ptosis and extraocular muscle weakness.

Cross-References

► Chronic Progressive External Ophthalmoplegia Plus Disease
► Kearns-Sayre Syndrome (KSS)

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Diplopia in Vertebrobasilar System Disease

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Synonyms

Vertebrobasilar atherothrombotic disease (VBATD); Vertebrobasilar insufficiency (VBI)

Definition

Vertebrobasilar system disease is a vasculopathy that affects the vertebral arteries and/or the basilar artery. Most commonly this arises because of total or partial occlusion secondary to atherosclerotic changes, thrombosis, arterial dissection, vasculitis, or embolic occlusion. Additionally, diplopia can also be caused by dolichoectasia or elongation/distension of these vessels. Given that these arteries directly or indirectly feed the midbrain, pons, medulla, and part of the occipital lobe, neuro-ophthalmic manifestations of this disease are common. Patients with VBI can experience transient diplopia when cranial nerves 3, 4, or 6 are affected, from internuclear or supranuclear brain stem disorders, or from skew deviation. Typically patients with VBI have other neurologic symptoms that help localize to the brain stem.

Cross-References

► One-and-a-Half Syndrome

Further Reading

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Diplopia Monocular

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Synonyms

Monocular polyopia

Definition

Diplopia is a another name for double vision. There are two main types of diplopia: monocular and binocular. Monocular diplopia occurs under monocular viewing conditions with one eye only and binocular diplopia occurs under binocular viewing. If either eye is covered and the double vision still persists, then it is likely to be monocular diplopia and generally not of neurologic origin (some exceptions like cerebral polyopia and palinopsia occur however). Monocular, or non-strabismic, diplopia can be caused by several optical problems.

As stated above, the noticeable form of the condition is mostly optical in nature. Most commonly, dry eyes, astigmatism, and spherocylindrical refractive errors are to blame. Sometimes, monocular diplopia can arise from an extrapupillary aperture as seen in a surgical or laser iridectomy or iridotomy. The lens can be the culprit as seen in cataracts or lens displacements/subluxations. Corneal etiologies for monocular diplopia include keratoconus (a degenerative, cone-shaped cornea due to genetic, cellular, and environmental conditions) and lower level and higher level aberrations that may be due to corneal or lenticular etiologies. Chalazion producing lid

and cornea pressure can also cause monocular diplopia. The pinhole might be useful in eliminating monocular diplopia and establishing an intraocular etiology for the symptoms.

Cross-References

- ▶ Astigmatism
- ▶ Chalazion
- ▶ Keratoconus

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Diplopia, Restrictive Syndromes Causing

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Definition

Diplopia, or double vision, can be caused by multiple mechanisms. There are several situations in which diplopia is caused by restriction in the extraocular muscles (EOM). Congenital fibrosis of the EOM (e.g., medial rectus muscle restriction causing esotropia in children) can produce ophthalmoplegia and diplopia. Orbital myositis, a form of idiopathic orbital inflammation, is a benign, noninfectious condition that typically presents with pain, periorbital edema, erythema, and diplopia. Nonsteroidal anti-inflammatory or corticosteroid drugs are the mainstay for therapy. Thyroid eye disease may also produce restrictive diplopia. In Graves' disease thyroid-stimulating immunoglobulins bind to the thyroid producing hyperthyroidism but also cross-react with fibroblasts in the orbit causing a conversion to adipocytes. These accumulate and cause an inflammatory response and affect EOM. In trauma situations, a medial orbital wall or orbital floor fracture could cause entrapment of the medial rectus or inferior rectus muscles respectively. Postsurgical esotropia is an iatrogenic restrictive damage to EOM that may cause diplopia after sinus surgery.

Cross-References

- ▶ Chronic Progressive External Ophthalmoplegia Plus Disease
- ▶ Myasthenia Gravis, Overview
- ▶ Thyroid Eye Disease

Further Reading

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Direct Lens Block Angle Closure

▶ Ciliary Block (Malignant) Glaucoma, Muscarinic Antagonists for

Direct Siderosis

▶ Rust Ring, Iron Foreign Body Causing

Disability Glare

▶ Glare, General

Disability Glare Testing

▶ Glare Testing

Disc Hyaline Bodies

▶ Pseudopapilledema: Disc Drusen

Disciform Degeneration

▶ Disciform Scar

Disciform Disease with Endotheliitis

▶ Disciform Keratitis, Herpes Simplex Virus Causing

Disciform Edema

▶ Disciform Keratitis, Herpes Simplex Virus Causing

Disciform Keratitis, Herpes Simplex Virus Causing

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Synonyms

Disciform disease with endotheliitis; Disciform edema; HSV endotheliitis; HSV keratitis; Keratitis disciformis

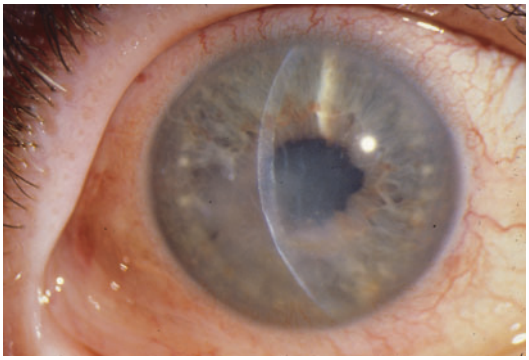
Definition

Herpes simplex virus (HSV)-induced disciform keratitis is a non-necrotizing keratitis of the cornea thought to be due to a delayed hypersensitivity reaction that manifests primarily as a localized endotheliitis with disk-shaped stromal and epithelial edema in a central or paracentral distribution (Krachmer et al. 2006; O'Day 2006).

Etiology

The main route of infection with HSV is through direct contact with mucous membranes. Ocular infection can occur as primary or recurrent episodes although HSV keratitis is thought to occur more commonly in recurrences. Primary ocular HSV typically presents as a blepharoconjunctivitis, while recurrent infection can occur on almost any ocular tissue including the eyelid, conjunctiva, cornea, iris, uveal tract, trabecular meshwork, retina, and optic nerve. In addition to endotheliitis, other manifestations of HSV with corneal involvement include epithelial keratitis, neurotrophic keratopathy, interstitial stromal keratitis (non-necrotizing), and necrotizing stromal keratitis (O'Day 2006).

Disciform keratitis is thought to be an immunologically driven reaction to the herpes simplex virus although there is some debate about the role of live virus in this reaction. The principle mediators are CD4(+) Th1 cells in addition to neutrophils and antigen-presenting cells. Cytokines such as interleukin 2 (IL-2), IL-12, and interferon gamma as well as IL-1alpha and IL-6 have been demonstrated to have activity in the inflammatory reaction (Inoue 2008). This immune reaction presents clinically with disk-shaped areas of epithelial and stromal edema with underlying fine keratic precipitates and is commonly associated with an iridocyclitis which may cloud the diagnosis (Fig. 1). The stromal edema and keratic precipitates appear out of proportion to the degree of anterior chamber reaction and can help distinguish the disciform keratitis from uveitis associated with secondary corneal decompensation. Although typically self-limited, ophthalmic steroids can speed recovery (O'Day 2006). Rarely,



Disciform Keratitis, Herpes Simplex Virus Causing, Fig. 1 Disciform keratitis. Note the clear periphery and well-demarcated areas of disk-shaped edema with underlying keratic precipitates (Image Credit: Dr. Richard K. Forsterp MD)

chronic endotheliitis may lead to intractable corneal edema secondary to the loss of endothelial cells, with resultant permanent scarring and neovascularization (Krachmer et al. 2006; Yanoff and Duker 2009).

Occurrence

HSV-1 exposure increases with age. Exposure is almost universal by the age 60 and was found on autopsy in the trigeminal ganglion 89.1% of the time by polymerase chain reaction (PCR). Although the virus may remain latent and without associated pathology, HSV keratitis is the most common cause of cornea-derived blindness in developed nations. The global incidence of Herpes keratitis is estimated to be approximately 1.5 million new cases each year (Farooq and Shulka 2012).

Classification

HSV disciform keratitis has traditionally been considered a stromal non-necrotizing keratitis and was included among the stromal keratitis in the Herpetic Eye Disease Study (Wilhelmus et al. 1994). However, HSV disciform keratitis is more appropriately described as an endotheliitis as the inflammatory reaction occurs primary at the level of the endothelium. This is supported by the observation that keratic precipitates (KP) are found on the endothelium only in areas of stromal edema and by the lack of stromal inflammation. More recent classifications now differentiate the types of HSV keratitis as primarily an epithelial disease with dendritiform lesions or neurotrophic ulcers, stromal necrotizing and non-necrotizing keratitis, or endotheliitis. Three forms of HSV endotheliitis are described: disciform, diffuse, and linear (Krachmer et al. 2006).

Cross-References

- ▶ Edema, Eyelid
- ▶ Herpes Simplex Virus
- ▶ Keratitis

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Disciform Scar

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Synonyms

Disciform degeneration

Definition

Disciform scar is an area of subretinal fibrosis or subretinal pigment epithelial (RPE) fibrosis. It is often located in the macula and is the end stage of neovascular age-related macular degeneration (AMD) Retina and vitreous (2014–2015).

Pathogenesis

Age-related macular degeneration (AMD) is the leading cause of worldwide blindness among the elderly. Clinically, AMD is classified into two types: the non-neovascular "dry" or atrophic form and the neovascular "wet" form.

The typical clinical sign of "dry" AMD is drusen, which are small yellowish deposits underneath the retina, found between the RPE and Bruch's membrane. In 15–20% of patients, the condition progresses to the "wet" or neovascular form. The natural history of wet AMD advances further to a cicatricial stage referred to as a disciform scar.

The hallmark of the neovascular form of AMD is the formation of choroidal neovascularization (CNV). These neovascular vessels originate from the choroidal capillaries, which progress and penetrate the outer aspect of Bruch's membrane. The neovascular complex continues to grow in the sub-RPE and subretinal space. The neovascular complex is accompanied by the growth of fibroblasts, resulting thus in proliferation of a fibrovascular complex within the inner aspect of Bruch's membrane. This complex can disrupt and destroy the normal architecture of the choriocapillaris, the Bruch's membrane, the RPE, and the photoreceptors Retina and vitreous (2014–2015) .

Ultimately, if left untreated, within several months, this process results in a 4–8 mm diameter fibrotic scar underlying the macula. On examination disciform scar appears as dull, white fibrous tissue which may include a vascular component. It can present concomitantly with CNV or replace the latter over time. Patients complain about central scotoma with severe central vision loss in the affected eye. However, peripheral visual acuity is usually retained.

To this current moment, no efficient treatment has been found to treat this condition Retina and vitreous (2014–2015).

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Disconnection Syndrome

▶ Alexia, Without Agraphia

Disodium Ethylenediaminetetraacetic Acid

▶ Chelation Therapy, for Calcific Band Keratopathy

Dispersion: Definition

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Synonyms

Abbe number; Wavelength-dependent refractive index

Definition

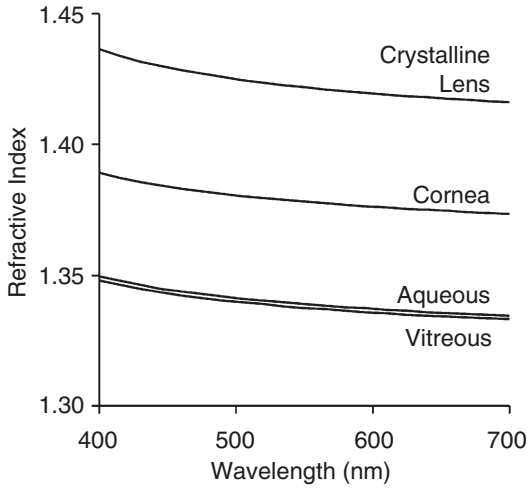
The refractive index of transparent media is dependent on wavelength, as illustrated in Fig. 1. As white light is incident upon a surface, the angle of refraction through the surface will depend on wavelength: the shorter wavelengths will refract more strongly than the longer wavelengths. This causes the separation of white light into its elemental colors through a prism, crystal, or water

droplets giving rise to a rainbow as shown in Fig. 2. The wavelength dependence of the refractive index also means that the eye and ophthalmic lenses have different focal lengths for different colors, leading to axial chromatic aberration (see ▶ Chromatic Aberration: Definition).

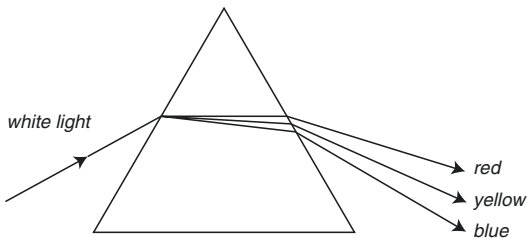
The dispersion of a material is quantified with the Abbe number, as defined below:

$$V = \frac{n_d - 1}{n_F - n_C}$$

where n_d, n_F, and n_C are a material's refractive index for wavelengths of 587.6, 486.1, and 656.3 nm, corresponding to helium *d*, hydrogen *F*, and *C* lines, respectively (Smith 2000).



Dispersion: Definition, Fig. 1 Chromatic dispersion curves for ocular media from Atchison and Smith (2005) based on the data of Le Grand et al. (1967) and Navarro et al. (1985)



Dispersion: Definition, Fig. 2 Chromatic dispersion of white light into its constituent wavelengths by a prism

Cross-References

▶ Chromatic Aberration: Definition

References

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D

Distichiasis: Definition

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Synonyms

Aberrant lash

Definition

Distichiasis is a condition where an extra row of eyelashes emerge at or slightly behind the meibomian gland orifices (Vagefi et al. 2011). In order from posterior to anterior lid margin, the normal anatomic structures are palpebral conjunctiva, mucocutaneous junction, gray line, meibomian glands, and eyelashes. Distichiasis can be congenital or more commonly acquired.

Congenital distichiasis is a rare condition that occurs when primary epithelial germ cells destined to differentiate into a meibomian gland of the tarsus develop into a complete pilosebaceous unit. The condition is inherited in an autosomal dominant manner with high penetrance, but it has

variable expressivity (Kanski 2007). Frequently, patients with congenital distichiasis will also be identified as having lymphedema-distichiasis syndrome. These individuals have distichiasis with lower extremity lymphedema that is usually asymmetric. These patients may also present with cardiac anomalies or a cleft lip (Boon and Vikkula 2012).

Aberrant lashes in congenital distichiasis can develop as either a partial or complete second row. In congenital cases, the aberrant lashes tend to be thinner and shorter than normal cilia. At a young age, the lashes tend to be finer and well tolerated. However, the lashes tend to be directed posteriorly and with time and age become coarser and can lead to corneal epithelial breakdown.

Acquired distichiasis is occurs when metaplasia of the meibomian glands leads to the formation of a hair follicle. This process is secondary to trauma or chronic irritation from inflammatory conditions of the eyelids or conjunctiva. Common causes include late stage cicatrizing conjunctivitis, chemical injury, Stevens-Johnson syndrome, ocular cicatricial pemphigoid, other chronic ocular surface diseases like blepharitis, or ocular rosacea. Aberrant lashes in these cases can also be directed posteriorly toward the cornea and cause epithelial breakdown. Acquired distichiasis usually becomes symptomatic.

Cross-References

- ▶ Congenital Entropion
- ▶ Trichiasis

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DLEK

- ▶ Transplantation

DME

- ▶ Diabetic Macular Edema

DMEK

- ▶ Transplantation

DNA, Disorders with Retinal Phenotype, Associated with Mitochondrial DNA (mt-DNA) Mutations

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Synonyms

Mitochondrial-related retinal degenerations (MRDs)

Definition

Mitochondrial retinal degeneration (MRD) is a heterogeneous group of multisystem disorders including retinal involvement, which associates with mitochondrial DNA (mt-DNA) mutations (Merin 2005). The various subtypes of MRDs are commonly subdivided according to their accompanying systemic findings. The retina may manifest a spectrum of clinical appearances (phenotypes) ranging from peripheral involvement similar to retinitis pigmentosa (RP) to

macular involvement only. Nevertheless, based on the retinal findings alone, the distinction of a specific genetic etiology could not be made.

Etiology

The exact mechanisms for retinal involvement in mt-DNA mutations are not fully understood. Most researchers tie this propensity with dysfunction of important mitochondrial roles for cell function and survival including adenosine triphosphate (ATP) production, control of cellular metabolism, and regulation of the programmed cell death mechanism, i.e., apoptosis. As a high-energy-demand organ, the retina is particularly susceptible to the consequence of mitochondrial damage. The phenotype of most MRDs is influenced not only by the specific mt-DNA mutation but the contribution of other factors such as the mutant load (degree of heteroplasmy), age of onset, and the impact of other nuclear genes.

Clinical Presentations

The clinical manifestations of many MRDs share a significant phenotypic overlap, which may prohibit ready distinction of a specific genetic etiology based on clinical parameters alone (Merin 2005; Grönlund et al. 2010). To further complicate matters, a given mt-DNA mutation may associate with a spectrum of phenotypes. Below is a list of the major MRD subtypes. Their classification relies mainly on accompanying systemic findings rather than their retinal appearance.

- **Neurogenic weakness**, **ataxia**, **and retinitis pigmentosa** (**NARP**) – the term NARP highlights the major signs of the syndrome. It results from a point mt-DNA mutation T8993C (or T8993G), in the mitochondrial complex V subunit gene ATPase 6. Notably for this mutation, the ratio of the mutant DNA to all mt-DNA usually determines the clinical manifestation. An individual has a normal phenotype if the "mutant load" is less than 60%, while NARP associates with >60% "mutation load." When the "mutation load" exceeds 80%, a more severe phenotype termed Leigh syndrome may develop.

  The retinal phenotype is consistent with retinitis pigmentosa.
- **Leigh syndrome** – also designated maternally inherited Leigh syndrome (MILS), has a more severe and fulminant course than NARP which usually results with death at infancy. It is considered as a degenerative disorder involving the basal ganglia and brain stem. The child is born with hypotonia, psychomotor abnormalities, lactic acidosis, seizures, and ataxia.
- **Mitochondrial encephalomyopathy, lactic acidosis, and stroke** (**MELAS**) – the term highlights the main signs of the syndrome. The most common mutation causing MELAS is A3243G, but other mutations were also described (A3271G). Neurological abnormalities are the most common manifestations with variable phenotypic expressivity ranging from stroke-like episodes, mental retardation, and sensorineural hearing loss. Other systemic abnormalities such as lactic acidosis, myopathy, or diabetes were also described. The brain lesions may be slowly progressive. Headache is usually the first symptom followed by hemianopsia, psychosis, and aphasia with a later occurrence of seizures. The retinal phenotype may vary from peripheral involvement with atypical RP to maculopathy alone.
- **Maternally inherited diabetes and deafness** (**MIDD**) – as indicated by the name, MIDD is characterized by diabetes and sensorineural hearing loss (Murphy et al. 2008). The most common mutation described in MIDD is the same A3243G mutation described for MELAS despite the different appearances of the syndromes. The disease commonly starts at early adulthood with high-tone frequency hearing loss, which usually precedes the onset of diabetes. In most cases, a non-insulin-dependent diabetes mellitus (NIDDM) without overweight develops.

  In contrast to the peripheral retinal involvement in MELAS, the main ocular feature in MIDD is a localized pattern dystrophy of the macula.

- **Kearns-Sayre syndrome** (**KSS**) – is characterized by chronic progressive ocular motility deficit (CPEO, chronic progressive extraocular ophthalmoplegia) and pigmentary retinopathy of the "salt and pepper" type which may progress to exhibit full-blown RP appearance in late stages. The ophthalmoplegia usually starts with strabismus or eyelid drop (ptosis) which progresses to complete (or almost total) paresis of the extraocular muscles. Accompanying multisystem abnormalities may include various CNS dysfunctions (ataxia, mental retardation, sensorineural hearing loss, high CSF protein content) and cardiac conduction block. KSS usually starts at early age (adolescence) and usually results in early death.

  The disorder associates with large deletions, duplications, or rearrangement of mt-DNA.
- **Myoclonic epilepsy and ragged red fibers syndrome** (**MERRF**). The acronym highlights the more common findings in MERRF which include myoclonus, ataxia, and the appearance of ragged red fibers on muscle biopsy. Other less frequent features include hearing loss, exercise intolerance, peripheral neuropathy, dementia, optic atrophy, and a mild retinal pigmentary disorder. The most common mutation A8344G is present in 80–90% of the patients with MERRF and encodes for the mt-RNA Lys gene.

Diagnostics

The diagnosis of MRD is established on clinical and laboratory grounds (Merin 2005; Haas et al. 2008). A common symptom of mitochondrial disease is fatigue. Typically, there is an increased blood lactate/pyruvate ratio following exercise. Maternal inheritance is characteristic, as mt-DNA is almost exclusively inherited from the mitochondria of the maternal oocyte during embryogenesis. These features, alongside any of the clinical presentations listed above, raise the likelihood for MRD. Confirmation of the diagnosis can be supported by muscle biopsy, MRI studies, and molecular screening for mt-DNA mutations.

Therapy and Prophylaxis

At present, no medication has been proven to alter the course of MRD. Evidence for the effectiveness of dietary supplementation, antioxidants, and vitamins remains controversial. There are a variety of reproductive options available for women with mt-DNA mutations including genetic counseling, ovum donation, antenatal diagnosis (by CVS biopsy), and preimplantation genetic diagnosis.

Prognosis

Generally, MRDs are considered progressive incurable disorders which may result in severe debilitating conditions or even death.

Epidemiology

MRDs are very rare, with an estimated occurrence rate approximating 1 out of 8,000–10,000 individuals.

Cross-References

▶ Atypical Retinitis Pigmentosa (RP)

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Doll's Eye Movement

▶ Doll's Head Maneuver/Phenomenon, in Horizontal Gaze Palsy

Doll's Head Maneuver/Phenomenon, in Horizontal Gaze Palsy

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Synonyms

Doll's eye movement; Oculocephalic reflex

Definition

The doll's eye maneuver is executed by quickly turning the patient's head horizontally from side to side or vertically up and down while holding the eyelids open. If the reflex is intact (positive doll's head maneuver), then the eyes demonstrate conjugate movement in the opposite direction of the head movement; however, if the reflex is not intact (negative doll's head maneuver), then the eyes remain stationary (Hickey 2003).

Purpose

This maneuver evaluates the functioning of the brain stem vestibular ocular reflexes and can help differentiate between supranuclear (e.g., cortical or subcortical dysfunction) in vertical or horizontal gaze palsies in both conscious and unconscious patients (Hickey 2003; McInery 2009).

Principle

Stimulation of the vestibular system by passive head movement causes eye movement without the involvement of the cortex. Upon turning of the head, afferent nerve fibers from the vestibular system stimulate specific ocular motor cranial nerve nuclei located in the brain stem, allowing for conjugate eye movement in the opposite direction of head movement (Haines 2012). More specifically, the movement of the head in the vertical direction will stimulate the trochlear and oculomotor nerves, whereas the movement of the head in the horizontal direction stimulates the abducens and oculomotor nerves. A negative doll's head maneuver indicates damage of the infranuclear pathway (Hickey 2003). On the other hand, a positive oculocephalic reflex in combination with a vertical or horizontal gaze palsy indicates that the lesion is supranuclear (McInery 2009).

Indication

The doll's head maneuver is used to test the brain stem functioning in comatose patients and neonates, and it can also be used in the initial evaluation of supranuclear versus infranuclear strabismus or other gaze palsies (McInery 2009; Venes 2013).

Contraindication

In the presence of cervical fracture or injury, this maneuver should not be performed (Hickey 2003).

Advantage/Disadvantage

The primary advantage to this maneuver is that it is a quick method of assessing brain stem function in a comatose patient. However, this test can only

be a preliminary evaluation because it does not provide precise localization of lesions or deficits (Hickey 2003).

Cross-References

► Efferent Visual System (Ocular Motor Pathways)

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Dominant Familial Drusen

► Doyne's Honeycomb Dystrophy

Dominant Optic Neuropathy (DOA)

► Mitochondrial Optic Neuropathy

Dorsal Midbrain (Parinaud) Syndrome, Convergence-Retraction Nystagmus, Eyelid Retraction

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Synonyms

Koerber-Salus-Elschnig syndrome; Parinaud's syndrome; Pretectal syndrome; Sylvian aqueduct syndrome

Definition

The dorsal midbrain syndrome is also known as the Parinaud syndrome, named after the notable nineteenth century French ophthalmologist Henri Parinaud who was the first to describe the cardinal clinical features of the disorder. The syndrome classically consists of a supranuclear paralysis of vertical gaze (predominantly upgaze initially but later downgaze may become involved), convergence-retraction nystagmus, and impaired pupillary constriction to light stimuli but normal to near reaction (i.e., light-near dissociation).

Etiology

Lesions of the dorsal midbrain (pretectal area) may also variably affect the medial longitudinal fasciculus (MLF), the superior colliculus, the pretectal nucleus, and the posterior commissure. Damage to these structures produces the classic signs associated with the syndrome. The most common causes are pineal mass (e.g., pinealoma, dysgerminoma, metastasis), vascular lesions (e.g., ischemia, hemorrhage, infarct, or arteriovenous malformations,), demyelinating disease (e.g., multiple sclerosis),

trauma, obstructive hydrocephalus or shunt failure, metabolic disorders (Wilson disease), and infectious (e.g., Whipple disease, tuberculosis, infective endocarditis, neurosyphilis) or inflammatory (e.g., neurosarcoidosis) etiologies.

Clinical Presentation

Vertical gaze (particularly upgaze) palsy is common in the dorsal midbrain syndrome. Patients may initially have a difficult time looking upwards voluntarily and eventually experience significant difficulty following an object upwards with their eyes. The absence of convergence and pupillary constriction reflexes can also be noted (with preservation of the near-pupillary response), as the neural projections that control these eye movements synapse at the site of the lesion implicated in the syndrome. Patients frequently complain of difficulty reading or double vision (diplopia) since both convergence and accommodation are disrupted.

In contrast, horizontal gaze is typically preserved because the ocular motor pathways controlling horizontal eye movements utilize nuclei and ascending tracts projecting from the rostral pons and not the midbrain. The vestibulo-ocular reflex is also preserved because the necessary neuronal connections for this reflex arise rostrally in the brain stem, away from the site of the lesion.

Convergence-Retraction Nystagmus

Convergence-retraction nystagmus is a classic dorsal midbrain sign and is best observed when patients attempt upward saccades, as when following a downward-moving optokinetic drum. The eyes then converge and retract into the orbit from co-contraction of the medial, superior, and inferior recti muscles bilaterally in attempted upgaze.

Eyelid Retraction

In patients with dorsal midbrain syndrome, the upper eyelids may be retracted. When this occurs, the superior sclera can be seen above the limbus (Collier sign). The cause of this sign is probably damage to levator inhibitory fibers in the posterior commissure.

Diagnostics

Magnetic resonance imaging (MRI) of the brain with and without gadolinium enhancement is typically the best initial neuroimaging study, but computed tomography (CT) scan of the brain without contrast may be faster in the traumatic or emergent setting. Lumbar puncture and serologic testing (e.g., syphilis) may be necessary for other etiologies if neuroimaging is negative.

Differential Diagnosis

Pineal tumors, progressive supranuclear palsy, bilateral Brown superior oblique tendon sheath syndrome, congenital upgaze limitation, transtentorial herniation, infections (encephalitis, cysticercosis), Wernicke encephalopathy, stroke – ischemic or hemorrhagic, and multiple sclerosis. Thyroid ophthalmopathy and myasthenia may mimic the ophthalmoplegia of the dorsal midbrain syndrome.

Therapy

Treatment should be directed against the underlying cause.

Prognosis

Prognosis for dorsal midbrain syndrome depends on the underlying etiology.

Epidemiology

Dorsal midbrain syndrome is a rare disorder that occurs in patients of all ages, and various etiologies may be more common in younger (e.g., demyelinating) or older (e.g., ischemic) patients.

Cross-References

▶ Parinaud (Dorsal Midbrain) Syndrome
▶ Setting Sun Sign

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Dorsal Midbrain Syndrome

► Parinaud (Dorsal Midbrain) Syndrome

Double Convexity Deformity

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Definition

Age-related changes to the eyelid-cheek junction, resulting in replacement of the youthful single convex contour of the lower eyelid and midface unit by a double convex contour with anterior bulging of the postseptal lower eyelid fat, descent of the midface, and volumetric deficiency in the region of the orbitomalar ligament (Baker 1999; Aston et al. 2009; de Castro and Boehm 2009).

Etiology

In youth, the lower eyelid and midface forms a single convexity, beginning at the inferior margin of the lower eyelid in the pretarsal region and extending inferiorly to the lateral oral commissure and angle of the mandible. By the third decade, the suborbital orbicularis oculi fat (SOOF) and the cheek fat pad typically descend, resulting in a soft tissue paucity inferior to the inferior orbital rim. In addition, with increased age, the globe moves inferiorly in the orbit, causing anterior bulging of the postseptal lower eyelid fat. The combination of bulging postseptal lower eyelid fat, soft tissue paucity at the inferior orbital rim, and inferiorly displaced SOOF and cheek fat pad form the classic double-convexity deformity.

Clinical Presentation

Patients present with a cosmetically unacceptable change in the contour of the lower eyelid and midface, typically in the third and fourth decade of life.

Diagnostics

The diagnosis of double-convexity deformity is made by clinical examination of the eyelid-cheek junction.

Differential Diagnosis

Differential diagnosis includes

Thyroid eye disease
Orbital tumor
Preseptal cellulitis
Allergic dermatitis/contact allergy to the eyelids

Therapy

Surgical correction of the double-convexity deformity may involve a variety of techniques and should be tailored to the patient's particular anatomy, with the goal of repositioning lower eyelid and midface soft tissues into a more aesthetically pleasing youthful configuration. Various surgical techniques in addition to lower eyelid blepharoplasty have been described such as arcus marginalis release, fat mobilization, and/or orbicularis oculi resuspension. Hyaluronic acid and non-hyaluronic acid filler

injection may also play a role in reconstructing mid-facial contour. Fat grafting is an option for volumetric rejuvenation in selected patients.

Prognosis

Double-convexity deformity is typically progressive with age, but does not result in functional compromise. Outcomes after surgical correction are variable and depend on the surgical technique employed.

Epidemiology

Unknown

Cross-References

- ▶ Infraciliary Blepharoplasty Incision, for Anterior Orbitotomy
- ▶ Iris Prolapse

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Double Ring Sign: Optic Nerve Hypoplasia

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Definition

The "double ring sign" is a characteristic configuration of the optic nerve head that is observed upon funduscopic examination in patients with optic nerve hypoplasia (ONH). The sign appears as a peripapillary yellowish, mottled halo that surrounds the hypoplastic optic disk. In ONH, there is a decreased number of optic nerve axons with normal amount of supporting tissue. The outer ring of the double ring sign represents the junction between sclera and lamina cribrosa, while the inner ring is the termination of the retinal pigment epithelium (RPE). The inner ring often appears whitish due to the glial and connective tissue around the retinal vessels. In ONH, the size of the smaller optic nerve plus the peripapillary halo may be roughly the size of a healthy optic disk. Other features that may be apparent include tortuous non-dilated retinal veins, decreased foveal reflex, and decreased thickness of the retinal nerve fiber layer. ONH on exam can range from dramatic findings if the optic disk appears to be one-half or less of the normal size and is accompanied by the double ring sign to much more subtle changes, necessitating detailed evaluation of the nerve under higher magnification before diagnosis can be confirmed.

Etiology

ONH is a congenital malformation of prenatal origin. ONH may present during evaluation of a unilateral visual defect, an examination of

strabismus, nystagmus, amblyopia, or unusual appearance of optic disk. ONH may present unilaterally or bilaterally with variable effect on vision. While there is no single unifying theory to explain the pathophysiology underlying ONH, the usage of certain recreational substances as LSD and ethanol (fetal alcohol syndrome) and certain classes of therapeutic drugs such as anticonvulsants and diuretics has been associated with the disorder, as has diabetes mellitus in expectant mothers. ONH is often accompanied by developmental delay, cerebral palsy, seizures, and a variety of neurodevelopmental and central nervous system (CNS) abnormalities and pathologies. One hypothesis for the etiology of ONH is excess apoptosis during embryonic ganglion cell and axonal development from abnormal mitochondrial function and energy metabolism. Another hypothesis is that ONH is the outcome of an initially reduced number of retinal precursor cells that eventually become retinal ganglion cells. The most important intervention in ONH may be the identification of associated endocrinopathies or CNS abnormalities to allow for early treatment and minimization of complications.

Occurrence

The double ring sign is quite common among patients with ONH but not always present and is not necessary for the diagnosis. ONH is the most common optic disk anomaly seen in clinical practice. The disorder itself occurs between 4% and 13% among children in US schools for the blind. In Finland, the prevalence of ONH has been estimated at 1.5 per 100,000 individuals (and a 4% prevalence among visually impaired children). In Sweden, the prevalence has been estimated to be at least 7 per 100,000 births.

Classification

Histopathologic sign.

Cross-References

► Optic Nerve (Cranial Nerve II)

Further Reading

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Downward Ocular Deviation

► Setting Sun Sign

Doyne Dominant Drusen

► Doyne's Honeycomb Dystrophy

Doyne Honeycomb Degeneration of Retina

► Doyne's Honeycomb Dystrophy

Doyne's Honeycomb Dystrophy

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Synonyms

Autosomal dominant drusen; Dominant familial drusen; Doyne dominant drusen; Doyne honeycomb degeneration of retina; Malattia Leventinese (ML)

Names in previous usage include Hutchinson-Tay choroiditis and Holthouse-Batten chorioretinitis.

Definition

DHRD is an autosomal-dominant degenerative retinal disease characterized by drusen (small round deposits of extracellular material located between the basement membrane of the retinal pigment epithelium (RPE) and the collagenous layer of Bruch's membrane). Those primarily at the macula coalesce in time to form a central solid plaque at the level of Bruch's membrane surrounded by smaller drusen deposited in a radial distribution (Brown et al. 2006). Drusen are also located characteristically in the nasal retina and around the optic disk (Fig. 1).

Etiology

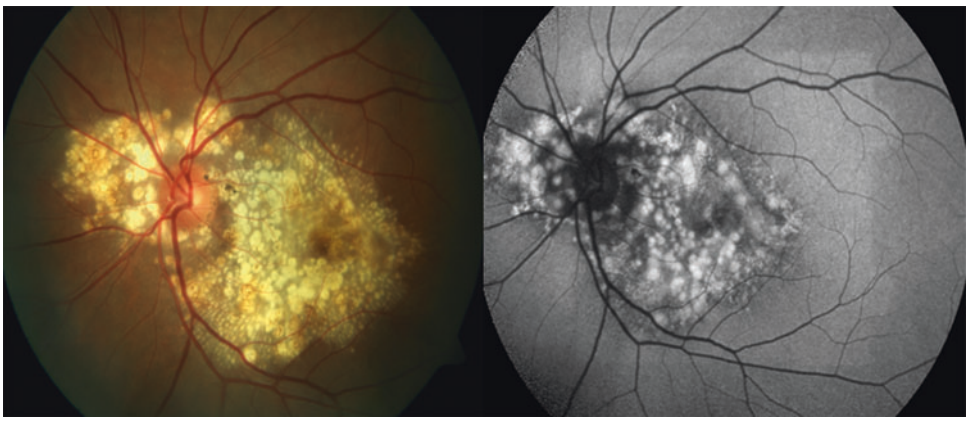
DHRD is caused by a single heterozygous pArg345Trp (R345W) mutation in the fibulin 3 gene, also known as the EGF-containing fibulin-like extracellular matrix protein 1 (EFEMP1), an extracellular protein localized to RPE (Stone et al. 1999). Not all patients with early onset retinal drusen have a mutation in the fibulin 3 gene, but with an autosomal-dominant history and the typical radial drusen as well as nasal and peridisc distribution of drusen, this makes it much more likely that they will be mutation positive.

Clinical Presentation

DHRD may be identified by examining members from a family with known DHRD, or patients may be asymptomatic, but referred because of early onset drusen. Onset of symptoms of delayed dark adaptation can occur before onset of distortion, blurring, or scotomata, which do not usually occur before the third to fifth decade (Haimovici et al. 2002). Early-onset macular drusen may be sparse at first; the distribution of the drusen in the nasal retina and around the optic disk together with a positive family history should arouse suspicion of DHRD. The macular drusen demonstrate a symmetrical bilateral radial distribution with increasing density of central deposition and coalesce to form the characteristic honeycomb pattern of RPE, developing a central plaque with supervening atrophic change and hyperpigmentation. Choroidal neovascularization may also develop.

Diagnosis

The diagnosis is suggested by early-onset drusen with a positive family history and typical fundus findings, and in the majority with the specific phenotype, a mutation in the EFEMP1 gene will be identified.



Doyne's Honeycomb Dystrophy, Fig. 1 Color photograph (**a**) and autofluorescence (**b**) of a patient with EFEMP1-positive DHRD. Note the characteristic feature of drusen nasal to and surrounding the optic disk

Differential Diagnosis

Drusen seen in early age-related macular degeneration particularly with a family history
- Early-onset drusen
- Sorsby fundus dystrophy
- Pattern dystrophy
- Stargardt disease
- Best disease
- North Carolina macular dystrophy

Prophylaxis

There is no current prophylaxis, but advice regarding a good diet and smoking cessation is likely to be of benefit. Prophylactic photocoagulation aimed at reducing the number of drusen has been tried with some success (Lenassi et al. 2013).

Therapy

There is currently no established therapy for DHRD; however, intravitreal anti-vascular endothelial growth factor therapy is currently the most likely to be helpful in treating associated choroidal neovascularization (Sohn et al. 2011). As with other inherited retinal degenerations, genetic counseling should be offered prior to mutational analysis.

Prognosis

The majority of patients will not experience noticeable visual deterioration usually until the fourth or fifth decade. Visual loss is gradual until the RPE atrophy involves the foveal zone. Sudden vision loss may occur following choroidal neovascularization.

Epidemiology

DHRD equally affects both men and women. There are no clear prevalence data.

Cross-References

- ▶ Drusen
- ▶ Fundus Flavimaculatus (Stargardt Disease/Juvenile Macular Degeneration)
- ▶ Macular Dystrophy
- ▶ Retina, Structure of
- ▶ Retinal Pigment Epithelium

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Drops

- ▶ Ketorolac Tromethamine

Drug-Induced Headache

- ▶ Analgesic Rebound Headache

Drug-Induced Optic Neuropathy

► Toxic Optic Neuropathy
► Toxic/Nutritional and Hereditary Optic Neuropathy

Drugs, Ocular, Absorption of

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Definition

Absorption of a topical drug depends on its bioavailability. Increasing the amount of time the drug spends on the corneal surface improves drug absorption. This is influenced by the drug delivery system, which include gels, ointments, inserts, soft contact lenses, and collagen shields. Other factors that affect ocular drug absorption are nasolacrimal drainage, drug binding to tear proteins, drug metabolism by tear and tissue proteins, and drug diffusion across the cornea and conjunctiva. Absorption can also increase by disrupting the corneal epithelium.

Cross-References

► Light-Near Dissociation

Drugs: Anisocoria

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Definition

Anisocoria is defined as a difference in the size (diameter) of the two pupils. Common causes of anisocoria include iris damage (e.g., iris trauma or intraocular surgery), ocular sympathetic lesions (i.e., the Horner syndrome), and parasympathetic lesions (e.g., third nerve palsy, Adie tonic pupil). This chapter deals with drugs that cause anisocoria.

Etiology

Drugs that cause pharmacologic mydriasis include ocular parasympatholytics and sympathomimetics. These include topical, nasal, and sometimes systemic (which may have inadvertent contact with the eye) agents. Mydriatic parasympatholytic agents include tropicamide, scopolamine, cyclopentolate, and atropine derivatives, while sympathomimetics include epinephrine and norepinephrine. Miotic agents include topical pilocarpine and exposure to parasympathomimetics (e.g., anticholinesterases). Systemic agents used for motion sickness (e.g., transdermal scopolamine) or nebulized inhalation agents (e.g., ipratropium bromide) might also be inadvertently administered to the eye causing pharmacologic anisocoria.

Differential Diagnosis and Evaluation

The differential diagnosis of pharmacologic anisocoria includes Horner syndrome, third nerve palsy, iris damage, and Adie pupil. Topical pilocarpine 1% will not constrict a fully pharmacologically dilated pupil and can be used as a differentiating test for neurogenic etiologies for a dilated pupil (e.g., atropine exposure).

Classification

Side effect of pharmacotherapy.

Cross-References

- ▶ Adie's Tonic Pupil
- ▶ Cranial Nerve III (Oculomotor Nerve)
- ▶ Horner's Syndrome
- ▶ Miosis

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Drugs: Hallucinations

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Synonyms

Hallucinogen; Psychedelic drug

Definition

Psychedelic drugs may cause visual hallucinations as part of the "psychedelic experience." This might include distortions of vision, hearing, thought, emotion, and perception. Perceptual distortions in particular may affect the senses of sight, sound, touch, smell, and taste, producing hallucinations, which are perceptions without external stimulation of the relevant sensory organ.

Hallucinations may be the primary effect of a drug or a side effect of use. Some drugs associated with visual hallucinations include:

- Hallucinogens (e.g., dimethyltryptamine, harmine, ketamine hydrochloride, LSD, mescaline, nitrous oxide, phencyclidine hydrochloride (PCP), psilocybin, tetrahydrocannabinol (THC))
- Stimulants (e.g., amphetamine, cocaine, methylphenidate, atropine, scopolamine, cyclopentolate)
- Anti-Parkinsonian agents (amantadine hydrochloride, anticholinergic drugs, bromocriptine, levodopa, lisuride, mesulergine, pergolide mesylate)
- Antidepressants (amitriptyline hydrochloride, amoxapine, bupropion hydrochloride, doxepin hydrochloride, imipramine hydrochloride, lithium carbonate and phenelzine sulfate)

Classification

Primary effect or side effect of pharmacotherapy.

Cross-References

► Hallucination

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Druse – Singular Form

► Drusen

Drusen

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Synonyms

Druse – singular form

Definition

Drusen are discrete whitish-yellow deposits of abnormal material located deep to the retina between the basal lamina of the retinal pigment epithelium (RPE) and Bruch's membrane. Varying widely in number, size, and shape, drusen can be confined to the macula region or involve large portions of the retina. The presence of drusen is suggestive of age-related macular degeneration although other diseases such as familial dominant drusen or basil laminar drusen also can be associated with drusen.

Cross-References

► Age-Related Macular Degeneration
► Doyne's Honeycomb Dystrophy

Dry Eye

► Keratoconjunctivitis: Overview

Dry Eye Disease

► Keratoconjunctivitis, Sicca: Definition

Dry Eye Syndrome

► Keratoconjunctivitis: Overview

Dry Eye: Definition

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Synonyms

Dysfunctional tear syndrome; Keratoconjunctivitis sicca

Definition

Dry eye is a common condition involving abnormalities of the tear film due to insufficient tear production or increased tear evaporation (Lemp et al. 2007). Symptoms include ocular discomfort such as dryness, foreign body sensation, or burning in the eye, visual disturbances, and tear instability. Dry eye is one of the leading causes of patient visits to ophthalmologists (Asbell and Lemp 2006).

Cross-References

- ▶ Keratoconjunctivitis Sicca
- ▶ Schirmer Tests
- ▶ Tear Breakup Time

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DSAEK

- ▶ Transplantation

DSEK

- ▶ Transplantation

Duchenne Muscular Dystrophy Associated with Pigmentary Retinopathy

- ▶ Duchenne Muscular Dystrophy: Retinal Degeneration

Duchenne Muscular Dystrophy Associated with Proliferative Retinopathy

- ▶ Duchenne Muscular Dystrophy: Retinal Degeneration

Duchenne Muscular Dystrophy: Retinal Degeneration

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Synonyms

Duchenne muscular dystrophy associated with pigmentary retinopathy; Duchenne muscular dystrophy associated with proliferative retinopathy

Definition

Duchenne muscular dystrophy is the most common X-linked neuromuscular disorder with an incidence of 1 in 3,500 live male births. It is characterized by progressive proximal muscular weakness, loss of ambulation, and early death. The disease typically manifests before 3 years of age with 95% of patients wheelchair-bound by the age of 12 years, rarely reaching the third decade of life. Duchenne muscular dystrophy is caused by a mutation of the dystrophin gene located on the short arm of the X chromosome at Xp21.

The retina contains three of the seven known isoforms of dystrophin including full-length dystrophin (Dp427), Dp260, and Dp71. The Dp260 isoform localizes at the retinal photoreceptor terminal (in the outer plexiform layer); its deficiency results in abnormal neurotransmission between photoreceptor cells and ON bipolar cells. The Dp71 isoform localizes in the inner limiting

membrane and around retinal blood vessels, playing an unclear role in retinal vascular permeability.

Patients with Duchenne muscular dystrophy may demonstrate abnormal scotopic electroretinogram (ERG) configuration, termed electronegative ERG, in which the scotopic a-wave and b-wave amplitude ratio is greater than 1. The severity of this unique ERG configuration varies based on the precise genetic mutation. The electronegative ERG configuration, similar to that seen in congenital stationary night blindness patients and other ocular diseases, indicates defective neurotransmission between photoreceptor cells and ON bipolar cells. However, in contrast to other X-linked disorders with a reduced scotopic b-wave ERG amplitude, color vision, photopic ERG amplitudes, visual acuity, and extraocular muscle function usually remain normal in patients with Duchenne muscular dystrophy. Patients classically have a relatively normal fundoscopic exam, with a slight tendency toward focal macular hyperpigmentation. Rarely, massive proliferative retinopathy may occur, leading to rapid and severe loss of vision. This atypical phenomenon is thought to be the end result of a vasoendothelial growth factor-mediated response resulting from a combination of cardiac hypoperfusion, the absence of an anti-vasogenic effect of dystrophin and anemia.

Cross-References

► Night Blindness
► Photoreceptor Cells

Duction Test

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Synonyms

Forced duction test

Definition

The forced duction test is a test of extraocular muscle (EOM) function that can be used to differentiate between EOM weakness (i.e., paresis) and restriction (e.g., entrapment, enlargement, infiltration, or fibrosis of muscle). If the EOM is acutely paretic, it will move easily when pushed or pulled during the forced duction. A restricted EOM on the other hand will not move freely.

Purpose

The forced duction test is very important for the diagnosis of EOM palsies or restriction in some cases of acute strabismus.

Principle

First, topical anesthetic (e.g., tetracaine) is instilled at the area where the conjunctiva will be grasped. The patient is told to cover one eye (manually or with an occluder) and to look in the

direction of the muscle that is suspected to be impaired. The examiner then uses forceps for globe fixation at the limbus and attempts to move the eye or by pushing on the deviated eye with a cotton-tipped swab or pulling the conjunctiva with forceps. If the examiner is unable to move the eye freely then this is a positive forced duction and supports restriction of EOM.

Indication

Indications for forced duction testing may include trauma, endocrine, congenital restrictions (Brown syndrome, Duane syndrome, strabismus fixus, congenital fibrosis of extraocular muscles), postoperative restrictions of motility (after strabismus procedures, orbital surgery, repair of retinal detachment), transposition procedures, and orbital diseases such as tumors and inflammation.

Contraindication

The forced duction test is contraindicated in the case of confirmed or suspected open globe injury.

Advantage/Disadvantage

The forced duction test is generally short and relatively painless. It increases diagnostic accuracy and helps in deciding which surgical strategy to employ. Some patients will not cooperate with this test; however, and the vagal response may be stimulated leading to syncope. For these patients, the test is best done in the operating room before surgery. Furthermore, the test can be painful for some patients and difficult to interpret. In addition, patients with chronic paretic lesions may develop a contracture and produce a false-positive forced duction test.

Cross-References

► Forced Duction Test

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Duplex Ultrasonography

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Synonyms

Duplex ultrasound

Definition

Duplex ultrasonography is a two-step ("duplex") imaging modality that is a combination of pulsed Doppler ultrasonography and brightness-mode

(B-mode) ultrasonography. It depicts a gray-scale (brightness scale) image of underlying tissue that is used to visualize the architecture of the body part (via grayscale ultrasound) and a color-Doppler ultrasound that helps visualize movement in a structure such as arterial blood flow via spectral analysis.

Purpose

Using the frequency of the original sound wave and the frequency of a received echo, duplex ultrasonography can calculate the velocity of moving red blood cells. Increased velocity of blood usually indicates narrowing of an artery or a form of resistance such as atherosclerotic plaque. Hence, it can be used to detect the presence and severity of vascular stenosis or occlusion and may provide valuable information for operative planning.

Principle

A duplex ultrasonography scanning device uses a pulsed Doppler beam to calculate frequency shifts in a specific area (the sample volume) by determining from what depth reflected echoes are received. The transducer is gated to only receive echoes from the specified area along the path of the pulsed Doppler beam. The depth of the sample volume is determined from the B-mode image.

Indication

Duplex ultrasonography is a minimally invasive way to determine vascular pathology in central and peripheral veins and arteries before further testing or surgery is involved. Thus, it can be utilized in a variety of suspected local and systemic vascular-related conditions such as deep vein thrombosis (DVT). An ophthalmologic application, for example, is the visualization of carotid arteries to identify occlusion, stenosis, and ulceration at the bifurcation of the carotid arteries in amaurosis fugax (a transient monocular visual loss that can be due to reduced blood flow reaching the eye).

Contraindication

Generally, there are very few contraindications for duplex ultrasonography. Depending on the body site of use, there may be some practical limitations, however. For example, evaluation of the abdominal aorta using this technique may be complicated by a large abdomen, a significant amount of bowel gas, open wounds, fresh sutures, or dialysis catheters.

Advantage/Disadvantage

The main advantage of duplex ultrasonography is the accuracy and minimally invasive nature with which it can be used to map vascular disease. Furthermore, it is safer and simpler than other techniques, which makes it one of the first line studies in vascular surgical planning. The main disadvantage is that it is a more time-consuming method than other arterial studies. Additionally, the sensitivity of duplex ultrasonography is lower than conventional and magnetic resonance angiography.

Cross-References

▶ Ultrasonography, in Orbital Evaluation
▶ Ultrasound

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Duplex Ultrasound

▶ Duplex Ultrasonography

Dural Sinus Thrombosis

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Synonyms

Cerebral venous sinus thrombosis (CVST)

Definition

Cerebral venous sinus thrombosis (CVST) refers to the presence of a thrombus (blood clot) in the dural venous sinuses. These sinuses are critical for draining blood from the brain.

Etiology

CVST of the lateral or sagittal sinus or small cortical veins can occur due to complications of oral contraceptives, pregnancy, inflammatory bowel disease, infections such as meningitis, dehydration, postpartum or postoperative states, and patients who have thrombophilic or hypercoagulable conditions as in pancreatic or colon cancer, cachexia in infants, cyanotic congenital heart disease, antiphospholipid antibody syndrome, polycythemia, Behçet disease, sickle-cell anemia, protein C or S deficiencies, factor V Leiden mutation, homocysteinemia, antithrombin III deficiency, paroxysmal nocturnal hemoglobinuria, and prothrombin G20210 mutation (especially with oral contraceptive use). Certain drugs including tamoxifen, erythropoietin, and bevacizumab are also risk factors for development of thrombosis.

Clinical Presentation

Patients experiencing CVST may present with headaches (most frequent symptom), seizures, and focal neurologic signs such as paraparesis. As intracranial pressure increases due to obstruction of cerebrospinal fluid (CSF) flow back to venous circulation, the patient may complain of nausea, vomiting, and headaches. Papilledema may also be seen and CVST can mimic the presentation of idiopathic intracranial hypertension (IIH).

Cavernous Sinus Thrombosis

Patients with cavernous sinus thrombosis may present with chemosis, proptosis, and cranial nerve III, IV, V (ophthalmic), or VI findings. If the thrombus spreads to the inferior petrosal sinus, then cranial nerve VI, IX, X, or XI findings may be present.

Diagnostics

Computerized tomography (CT) imaging may be normal in patients with dural sinus thrombosis unless venous hemorrhage has occurred. Thrombosis of the venous sinuses is best apparent with magnetic resonance venography (MRV) or computerized tomographic venography (CTV). Alternatively, catheter angiography may still be required to visualize CVST. In the case of superior sagittal sinus occlusion, hemorrhagic infarcts or edematous congestion in the frontal or parietal lobes may be observed. Cerebrospinal fluid (CSF) pressure is increased and fluid may contain traces of blood. With transverse sinus occlusion, hemorrhagic infarct of the temporal lobe with edema may be observed. A "corkscrew" appearance of surface veins is seen with chronic thrombosis.

Differential Diagnosis

Stroke
Hemorrhage

Therapy

Systemic anticoagulation is typically recommended for CVST.

Prognosis

With appropriate treatment, dural sinus thrombosis generally may resolve successfully or be appropriately controlled medically. Total mortality is about 9.4% but approximately 88% of survivors make a substantial recovery. The rate of recurrence of CVST is low and is estimated at 2.8% (Dentali et al. 2006).

Epidemiology

Dural sinus thrombosis is a rare condition accounting for less than 1% of all strokes with peak incidence in adults in the third decade of life. Exact incidence is unknown but five to eight cases per year can be expected in a tertiary care center. It is more common in women than in men (Einhäupl et al. 2006).

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DUSN

▶ Baylisascaris procyonis (Raccoon Ascarid), Diffuse Unilateral Subacute Neuroretinitis

DWI

▶ Diffusion-Weighted MR Image

Dyschromatopsia

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Synonyms

Color blindness; Incomplete achromatopsia

Definition

Dyschromatopsia, meaning "color confusion", is a form of color blindness, a diminished or impaired ability to see certain colors. In contrast,

complete loss of color vision is termed achromatopsia. Thus, dyschromatopsia is sometimes known as incomplete achromatopsia. In individuals with color blindness, the ability to perceive one or more primary colors is either defective (anomalous) or absent (anopia).

Etiology

Dyschromatopsia can either be congenital or acquired, though it is most frequently an inherited condition. A congenital color vision defect is typically red-green in nature, while acquired defects are generally blue-yellow in character. The hereditary bases for tritanopia and tritanomaly are related to chromosome 7 and are autosomal dominant. Protanopia/protanomaly and deuteranopia/deuteranomaly are X-linked recessive disorders.

Clinical Presentation

Dyschromatopsia can be classified as anomalous trichromatism or congenital dichromatism. Each of these classifications has several subtypes depending on which color is affected. The two major types of color blindness that patients present with are red-green and blue-yellow forms.

Anomalous Trichromatism

In anomalous trichromatism, all three cones for red, blue, and green color perception are present but in abnormal proportions or with altered spectral sensitivity. Individuals who have this condition can distinguish fully saturated colors but have difficulty distinguishing colors at low saturation. Perception for one or two of the three primary colors is partially impaired. Individuals who have defective red color appreciation due to abnormal red cone distributions are termed protanomalous individuals. Those who have defective green and blue perception are termed deuteranomalous and tritanomalous, respectively. Protanomaly and deuteranomaly correspond to red-green color blindness, while tritanomaly corresponds to blue-yellow blindness.

Congenital Dichromatism

In congenital dichromatism, patients present with a total inability to perceive one of the three primary colors because of complete absence of the necessary photoreceptors. Such individuals are called dichromats. Naming convention follows that for anomalous trichromatism, those who have a complete red perception defect have protanopia and green and blue defects are called deuteranopia and tritanopia, respectively. Protanopia and deuteranopia correspond to major difficulty distinguishing between red and green hues, while tritanopia, extremely rare, corresponds to a total lack of blue retinal receptors.

Diagnostics

The diagnosis of dyschromatopsia can often be confirmed by color vision testing. The Farnsworth-Munsell (FM) 100 hue test and Farnsworth's panel D-15 can detect both red-green and blue-yellow defects. The city university test is derived from the 100 hue test and can also be used. Ishihara color plates (which are designed to detect red-green defects) and Hardy-Rand-Ritter (HRR) polychromatic plates (better for both red-green and blue-yellow defects) are more convenient for use in the clinic setting but are less sensitive and specific.

Differential Diagnosis

- Kjer dominant optic atrophy (if tritan color defect and slightly subnormal vision)
- Optic nerve disease (if errors in testing are characteristic of red-green blindness)
- Retinal disease (blue-yellow blindness errors)
- Glaucomatous optic neuropathy (initially causes blue/yellow deficits)
- Various effects of drugs (example is xanthopsia in digoxin toxicity)

Therapy

Currently there is no therapy available.

Prognosis

Congenital forms of color blindness remain static over time.

Epidemiology

Some incidence figures for dyschromatopsia are as high as 13% of the population. The X-linked color blindness occurs much more frequently in males than females with about 8% of males and less than 1% of females affected. Red-green disorders are X-linked recessive and thus mostly found in males, whereas both men and women can have tritan (blue-yellow) disorders. Protan disorders are present in about 1% of males. Deuteranomaly (red-green blindness) is the most common type of color blindness and affects approximately 5% of European males. Tritan disorders are extremely rare.

Cross-References

- ▶ Achromatopsia
- ▶ Anomalous Trichromats
- ▶ Color Blindness
- ▶ Dichromatic Vision

Further Reading

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Dysfunctional Tear Syndrome

▶ Dry Eye: Definition

Dyskeratosis

▶ Carcinoma In Situ, of Conjunctiva

Dyskeratosis Follicularis

▶ Darier Disease (Keratosis Follicularis)

Dysthyroid Ophthalmopathy

▶ Graves' Disease

Dysthyroidal/Thyroid-Associated Orbitopathy

▶ Graves Ophthalmopathy

Dystrophia Smolandiensis Variant

▶ Recurrent Corneal Erosion

E

Eales' Disease

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Synonyms

Presumed tuberculous retinal periphlebitis

Definition

Eales' disease is an uncommon, idiopathic inflammatory retinal vasculopathy that mainly affects the peripheral retina of otherwise healthy young adults in their second to fourth decade of life. The disease was first described in 1880–1882 by Henry Eales as a noninflammatory condition in young healthy male patients who presented with recurrent vitreous retinal hemorrhages and epistaxis. Subsequently, the condition has been redefined as a primarily inflammatory condition (Biswas et al. 2002).

The disease is characterized by an obliterative, progressive, peripheral retinal vasculitis, predominately periphlebitis that can lead to large areas of peripheral retinal non-perfusion, severe retinal ischemia, and neovascularization, resulting in repeat vitreous hemorrhages with or without retinal detachment. In some patients there are associated retinitis and vitritis, but in others there is very little or no inflammation.

Etiology

Eales' disease remains an idiopathic condition, though several underlying conditions have been proposed, resulting in a variable clinical presentation. Hypersensitivity to tuberculin protein has been heavily implicated in the pathogenesis of Eales' disease, and investigations using polymerase chain reaction (PCR) techniques have documented the presence of the mycobacterium tuberculosis genome in the vitreous fluid of more than 50% of Eales' disease patients. This has led some researchers to suggest renaming Eales' disease as presumed tuberculous retinal periphlebitis. Other factors linked to developing Eales' disease include the presence of human leukocyte antigens (HLAs) B5, DR1, and DR4; oxidative stress due to increased concentrations of reactive oxygen species, especially inducible nitric oxide; and possible associations with hypercoagulable states such as factor V Leiden thrombophilia and proliferative responses against retinal S-antigen (Biswas et al. 2013).

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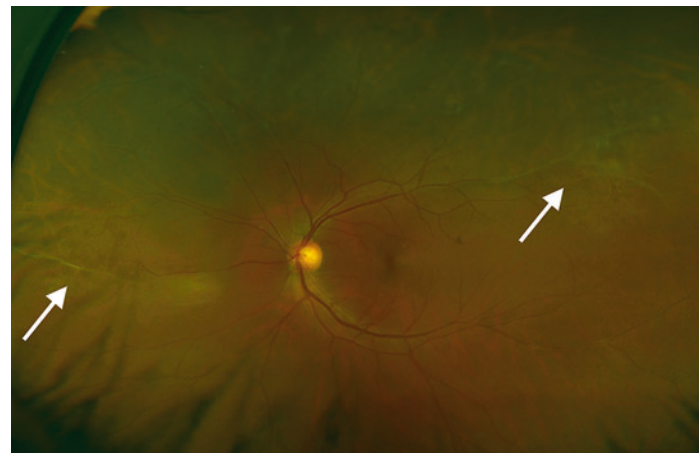
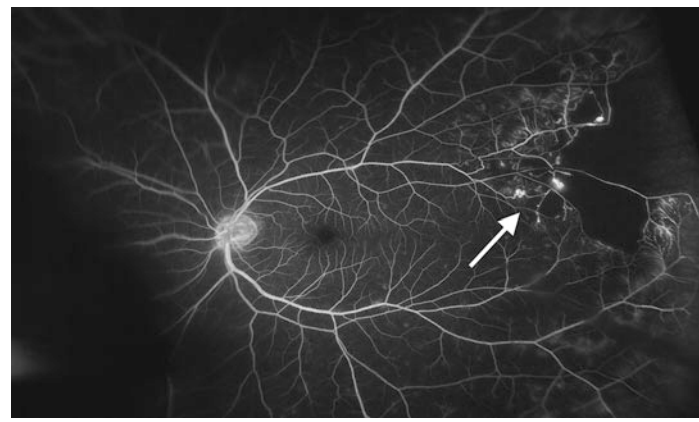
Clinical Presentation

Eales' disease occurs most often in young individuals, predominantly but not exclusively men in the second to fourth decade of life. Symptoms and clinical signs may be unilateral at presentation but eventually become bilateral in most cases. Typical symptoms include floaters secondary to vitritis or mild vitreous hemorrhage. Severe visual loss can occur with significant vitreous hemorrhage. There are three clinical hallmark characteristics to Eales' disease: retinal phlebitis (vasculitis), peripheral capillary non-perfusion, and recurrent vitreous hemorrhages (Figs. 1 and 2). Vitritis is present in some but not all eyes. Retinal phlebitis appears as mid-peripheral venous dilation, peripheral perivascular exudates, hemorrhages, and sheathing. Overlying vitritis can be seen in the area of active vasculitis, and the inflammatory reaction can result in cystoid macular edema and further vision loss. Capillary non-perfusion areas can be seen as peripheral areas with "ghost" vessels (obliterated thin white vessels). A demarcation line between the non-affected and affected peripheral retina can frequently be seen with some angiopathic changes such as microaneurysms, venular shunts, hard exudates, or cotton wool spots. Vitreous hemorrhage is most commonly caused by bleeding from neovascularization of the optic disk or retina secondary to the capillary non-perfusion, which may be very extensive.

The natural history of the disease is variable. Hemorrhages are usually the result of



Eales' Disease, Fig. 1 Eales' disease. Note the extensive areas of vascular occlusion and retina hemorrhages (*arrows*)



Eales' Disease, Fig. 2 Fluorescein angiography of patient in Fig. 1 demonstrating the large areas of retinal ischemia with neovascularization (*arrow*)

neovascularization, and these leaking vessels tend to regress (and regrow) spontaneously with resultant formation of a contractile scar tissue that can lead to traction retinal detachment. Patients who do not develop retinal detachments can achieve a stable state, where following recanalization, formation of capillary shunts, and tissue atrophy, the process of neovascularization, with the resultant vitreous hemorrhages, cease.

Diagnosis

Clinical examination will demonstrate peripheral retinal vasculitis with large areas of retinal ischemia, retinal hemorrhages, neovascularization, and vitritis in some. Fluorescein angiography (FA) is useful in identifying patterns of staining and diffuse leakage that correspond to the presence of peripheral vasculitis which may progress to cause areas of retinal ischemia and subsequent neovascularization. Areas of hypofluorescence with bordering engorged capillaries and venous shunts are seen in ischemic areas. Neovascularization can usually be seen along the area of retinal ischemia or the optic disk. Ultrasonography is needed to rule out the presence of a retinal detachment when vitreous hemorrhage obscures the fundal view.

Exposure to *M. tuberculosis* should be investigated in all cases suspected of Eales' disease (e.g., QuantiFERON gold, T-spot, Mantoux test, chest X-ray).

Differential Diagnosis

The main differential diagnoses are other retinal vasculitic diseases and other retinal diseases resulting in retinal neovascularization. Systemic diseases related to retinal vasculitis which may result in ischemia and neovascularization include tuberculous uveitis with vasculitis, Behçet disease, syphilis, sarcoidosis, systemic lupus erythematosus, and granulomatosis with polyangiitis. However, a careful history, clinical examination, and targeted diagnostic tests (blood investigations) will help rule out most of these causes.

Proliferative retinopathies without vasculitis include diabetes mellitus, sickle cell disease, branch and central vein occlusion, and previous retinopathy of prematurity.

Therapy

Corticosteroids when there are associated inflammatory signs (e.g., vitritis), together with antituberculous therapy and laser treatment to ischemic areas when there is neovascularization, are the mainstay of therapy in Eales' disease. In eyes with active vasculitis and vitritis, systemic corticosteroids are initiated to control the inflammatory reaction (prednisolone 1 mg/kg of body weight). The known association of Eales' disease with *M. tuberculosis* requires consideration of tuberculosis treatment, and in cases with a positive tuberculosis test, such treatment should be given for a period of 6–9 months even in the absence of clinically active systemic tuberculosis.

Retinal laser photocoagulation to areas of non-perfused retina and early vitrectomy for recurrent vitreous hemorrhages should be considered in the presence of neovascularization (Dehghan et al. 2005). The aim of photocoagulation is to reduce the ischemic drive that leads to the formation of neovascularization and induces new vessel regression in approximately 90% of cases (Gopal and Abraham 1985). Laser is given in a segmental scattered pattern to the areas of capillary non-perfusion. In the presence of optic disk neovascularization and extensive peripheral ischemia, panretinal photocoagulation is applied.

The use of intraocular bevacizumab has been suggested for inducing regression of neovascularization or in the management of traction retinal detachments, as an adjunctive treatment to vitreoretinal surgery. However, reports of an increased risk of progressive retinal ischemia require combining intravitreal bevacizumab with retinal laser photocoagulation in order to reduce the ongoing ischemic drive.

Prognosis

As Eales' disease is a peripheral retinal disease, many patients have a good visual outcome, even in the presence of extensive peripheral vascular occlusion. Satisfactory visual outcome has also been observed in eyes receiving laser photocoagulation, especially when combined with early vitrectomy. However, once advanced disease has occurred, including traction retinal detachment, macular ischemia, rubeosis iridis, neovascular glaucoma, and optic nerve atrophy, the visual prognosis is poor.

Epidemiology

While there is no racial predilection for Eales' disease, it has been mainly reported in India and parts of the Middle East. In these regions the prevalence of the disease was found to be up to 1 in 200–250 patients in India, as compared to one in 4800 in Great Britain (Gadkari et al. 1992). The disease mainly affects males (approximately 97% of cases) in their second to fourth decade of life.

Cross-References

► Neovascularization, Retinal

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Early Treatment Diabetic Retinopathy Study (ETDRS)

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Synonyms

Diabetic retinopathy; Early treatment of diabetic retinopathy study; ETDRS; Focal grid laser; Focal laser

Definition

The Early Treatment of Diabetic Retinopathy Study (ETDRS) was a randomized, prospective, multicenter, clinical trial designed to evaluate the role of aspirin and argon laser photocoagulation in patients with nonproliferative and early proliferative diabetic retinopathy (Ferris, study53.asp).

The Diabetic Retinopathy Study (DRS) previously showed that panretinal photocoagulation reduced the risk of severe vision loss (SVL 5/200 or worse vision) by 50% over 5 years in patients with high-risk proliferative diabetic retinopathy (DRS Report 8 1981). High-risk proliferative retinopathy was defined as either:

1. New blood vessel growth within one disk diameter of the optic disk (neovascularization of the disk) greater than one-fourth of a disk area in size with or without vitreous hemorrhage

2. Any new blood vessels on or near the optic disk with vitreous hemorrhage
3. New blood vessels in the retina (neovascularization elsewhere, NVE) greater than one-half disk area in size with vitreous hemorrhage (DRS Report 8 1981)

Given this finding, the ETDRS was only open to patients with less than high-risk PDR.

ETDRS preceded optical coherence tomography, so all grading of retinopathy was done either by fundus photographs, intravenous fluorescence angiography, or clinical exam with contact lens biomicroscopy or indirect fundoscopy. This limited the ability to detect and measure small amounts of macular edema. Macular edema was defined as clinically significant if it met one of the following three criteria:

1. Thickening of the retina within 500 um of the foveal center
2. Hard exudates within 500 um of the foveal center associated with thickening of the adjacent retina
3. An area of thickening greater in size than the one disk area located within one disk diameter of the foveal center

Moderate vision loss (MVL) was defined as a doubling of the visual angle or a loss of 15 letters on the logarithmic ETDRS vision chart (Basic and clinical science course retina and vitreous 2002–2003).

The ETDRS divided nonproliferative diabetic retinopathy into five groups:

1. No retinopathy.
2. Mild NPDR: Microaneurysms, venous loops, retinal hemorrhages, or hard exudates.
3. Moderate NPDR: Mild NPDR with cotton-wool spots and intraretinal microvascular abnormalities (IRMA) defined as abnormal blood vessels limited to the retina. Any neovascularization extending into the vitreous, on the optic nerve, or retinal surface was considered proliferative diabetic retinopathy.
4. Severe NPDR: Any one of the following without proliferative retinopathy (the 4-2-1 rule).
   More than 20 intraretinal hemorrhages in each of four quadrants
   Venous beading in two or more quadrants
   Prominent IRMA
5. Very Severe NPDR: Two of the above findings.

Quadrants were any one of four mid-periphery fields compared to seven standard 30° photographs. Grading was done by comparing to standard photographs (Ryan 2006).

Aims

- To test the effectiveness of aspirin and argon laser photocoagulation on progression of early diabetic retinopathy to visual loss and blindness
- To determine the optimal time to treat patients with photocoagulation
- To monitor the effects of photocoagulation treatment and diabetes on vision
- To follow the natural history of diabetic retinopathy and use that information to identify risk factors and to test etiologic hypotheses in diabetic retinopathy (Ferris, study53.asp)

Outcomes

The primary outcome was the percentage of patients with MVL at 4 years. Secondary outcomes included percentage of patients with severe vision loss (5/200) for 4 months or greater and progression of retinopathy.

Methods

A total of 3,711 patients were recruited and followed for a minimum of 4 years (Ferris, study53.asp). The study recruited patients from December 1979 to July 1985. The results were presented at the American Academy of

Ophthalmology meeting in New Orleans in 1989 (Ferris, study53.asp 2000; Kupfer, alert-etdrs.asp).

Enrolment Criteria

Patient ages ranged from 18 to 70 years old. Diabetic retinopathy varied from mild nonproliferative to mild proliferative retinopathy in both eyes. Best corrected visual acuity was 20/40 or better, unless macular edema was present, in which case 20/200 vision or better was allowed. No patients could have any history of prior photocoagulation (Ferris, study53.asp 2000).

All patients had one eye randomly assigned to observation or immediate focal grid photocoagulation. Patients were also randomly assigned to 650 mg aspirin or placebo (Ferris, study53.asp 2000).

Results

- Focal grid laser reduced the risk of moderate to severe vision loss in clinically significant macular edema by 50%. The 3-year risk of MVL without focal laser was 32% (Ryan 2006). Panretinal photocoagulation (PRP) was not effective in treating macular edema and led to a mild decrease in central and peripheral vision (Kupfer, alert-etdrs.asp).
- There was a low rate of severe vision loss at 5 years in both non-high-risk proliferative retinopathy treated with scatter photocoagulation (2.5%) and when treatment was delayed until the development of high-risk proliferative retinopathy (4%). Therefore, it was concluded that treatment could be delayed until high-risk characteristics developed, provided close follow-up can be maintained (Kupfer, alert-etdrs.asp).
- Treatment with 605 mg aspirin daily had no effect, either on the risk of vitreous hemorrhage or the progression of retinopathy (Kupfer, alert-etdrs.asp).
- Follow-up: Based on the ETDRS data, the recommended time for follow-up visits was determined for NPDR. The risk of developing HRPDR in 1 year was 0.8% for mild NPDR and 48.5% for severe NPDR. At 5 years, the risk was 14.3% and 74.4%, respectively. This was supported by the Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) (Ryan 2006). Therefore, the following recommendations were made for follow-up on diabetic screening based on grading of retinopathy:
  - No retinopathy: annual exam
  - Mild/Moderate NPDR without macular edema: 6–12 months
  - Mild/Moderate NPDR with macular edema but not CSME: 4–6 months
  - Severe or very severe NPDR: 3–4 month exam (Ryan)

Conclusions

The Early Treatment of Diabetic Retinopathy Study (ETDRS) was a major study that revolutionized the treatment of diabetic eye disease in the 1980s. While many of its contributions are now of historical importance, several important conclusions were reached by the study.

These include:

1. The use of aspirin in diabetic retinopathy did not affect the development or treatment of clinically significant macular edema nor did it affect the development of or response to therapy for proliferative diabetic retinopathy. There were no adverse effects, including no difference in the rate of vitreous hemorrhages. Therefore, aspirin is neither indicated nor contraindicated (Ryan 2006).
2. The timing of early panretinal photocoagulation (PRP): Patients with high-risk proliferative diabetic retinopathy (PDR) should be treated with PRP laser. Patients with non-high-risk PDR may be considered for early laser. PRP laser for patients with mild to moderate nonproliferative diabetic retinopathy was not indicated by the study.
3. The value of focal laser in the treatment of clinically significant macular edema: focal grid laser significantly reduced the rate of MVL in patients with CSME.

In addition, the study established:

(A) A grading system for grading diabetic retinopathy
(B) The use of logarithmic eye charts for checking visual acuity

These contributions have greatly affected future studies; however. the study and its results are limited in modern practice by the lack of optical coherence tomography (not commercially available until 20 years later) and anti-VEGF (Vascular endothelial growth factor) drugs, the two pillars of modern diabetic macular edema management.

Before ETDRS, the prognosis for patients with proliferative diabetic retinopathy was blindness within 5 years for more than 50% of patients. Rates of blindness in ETDRS patients following the development of proliferative retinopathy are remarkably lower. Legal blindness is reduced to less than 5% in 5 years for patients with proliferative retinopathy. Severe vision loss is reduced to 1%.

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Early Treatment of Diabetic Retinopathy Study

► Early Treatment Diabetic Retinopathy Study (ETDRS)

EBAA

► Eye Bank Association of America

Eccrine Acrospiroma

► Hidradenoma, Clear Cell (Eccrine Acrospiroma)

Eccrine Poroma

► Hidradenoma, Clear Cell (Eccrine Acrospiroma)

Eccrine Spiradenoma

► Spiradenoma, Eccrine

Eccrine Sweat Gland Adenoma

► Hidradenoma, Clear Cell (Eccrine Acrospiroma)

Echinococcus granulosus (Echinococcosis), Orbital

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Synonyms

Hydatid cyst

Definition

Human parasitosis caused by *Echinococcus granulosus*. Formation of hydatid cysts occurs most commonly in the liver, lungs, and central nervous system.

Etiology

Zoonosis caused by larvae or cestodes of the *E. granulosus* genus. The definitive hosts are dogs and other carnivores; cysts (metacestode stage) develop in sheep and cows. The larval stage develops in humans.

Clinical Presentation

In primary disease, patients usually present with unilateral findings. Usually found behind the globe or in the superior orbit causing slowly progressive proptosis. The cysts tend to grow slowly and cause orbital signs such as chemosis, pain, motility deficits, eyelid edema, optic nerve edema, vision loss, and optic atrophy. Rarely extension through the orbital roof into the intracranial cavity, or through orbital walls into the paranasal sinuses, may be seen.

Diagnostics

Clinical examination and orbital imaging with CT, MRI, and/or ultrasound. CT scan shows a well-defined, hypodense cystic lesion, with thin walls, and fine ring enhancement. May be unilocular or polycystic (5%). On MRI lesions appear low intensity on T1 and high intensity on T2. Capsular enhancement of the lesion is seen on T1 with gadolinium. Systemic eosinophilia is seen in 20–25%, and serologic testing may be negative in 50–60%.

Differential Diagnosis

Dermoid cyst, abscess, intraorbital hematoma, lymphangioma, teratoma, encephalocele, mucocele

Prophylaxis

Avoidance of endemic areas, hand hygiene, animal control measures, and possible immunization of animal hosts.

Therapy

Surgical excision without rupture of lesion is often difficult. Surgical excision with decompression and irrigation with hypertonic saline is used in many cases. Preoperative albendazole as preventative therapy for 14–28 days has been advocated. Concurrent treatment with anti-helminthic agents, such as albendazole, may be indicated.

Prognosis

Spillage of contents of cysts can lead to inflammatory reactions and systemic recurrence. Vision loss may be seen with delayed presentation, diagnosis, or severe disease.

Epidemiology

Endemic in cattle- and sheep-raising regions such as East and North Africa, Central Europe, the Middle East, India, Latin America, South America, Australia, and New Zealand. Orbital hydatid cysts are rarely encountered and comprise just 0.3–1% of all hydatid cysts. In endemic areas, hydatid cysts may be the cause of 5–26% of cystic orbital masses. The majority of patients are younger than 20 years of age. There is no gender predilection.

Cross-References

▶ Hydatid Cyst

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Eclampsia, Neuro-Ophthalmic Disorders, Transient Visual Loss

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Synonyms

Transient cerebral blindness; Transient cortical blindness

Definition

Eclampsia is a potentially life-threatening condition in pregnant women consisting of hypertension, generalized edema, proteinemia, and seizures. The prequel to eclampsia is preeclampsia, also known as pregnancy-induced hypertension (PIH), which consists of just the first three symptoms. Onset is usually after the 20th week of gestation. Visual complaints occur in approximately 40% of patients with preeclampsia. The most common complaints are blurring of vision, photopsias, scotomas, and diplopia. Other ocular manifestations include retinopathy, serous retinal detachments, optic neuropathy, and occipital cortical blindness. The most common ophthalmoscopic findings are retinal arteriolar narrowing, retinal hemorrhages, exudates, retinal vascular thrombosis, and retinal edema. Optic nerve changes associated with this condition include optic atrophy, papilledema, and anterior ischemic neuropathy. Transient visual loss, posterior reversible encephalopathy syndrome (PRES), or cortical blindness occurs in about 1–15% of patients with preeclampsia or eclampsia. In contrast to ischemic infarction, PRES is typically reversible and patients with PRES from eclampsia may recover vision between 2 h and 21 days with treatment.

Etiology

Petechial hemorrhage and focal edema develop from endothelial dysfunction, dysregulation of vascular autoregulatory mechanisms, and ischemia from vasospasm. Recovery of vision follows successful treatment and resolution of cerebral edema and underlying eclampsia with magnesium sulfate, fluid restriction, and blood pressure control.

Occurrence

The occurrence of transient visual loss or cerebral blindness is between 1% and 15% of patients with preeclampsia, PIH, or eclampsia. It is more common in very young and very old mothers, in first-time mothers, and in mothers with existing systemic disease such as diabetes, chronic hypertension, and renal disease.

Cross-References

▶ Diplopia in Multiple Sclerosis
▶ Retinal Detachment
▶ Transient Cortical Blindness

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Ecotrin

► Aspirin (for Carotid Artery Disease)

Ectasia, Corneal

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Synonyms

Iatrogenic ectasia; Keratectasia; Keratoectasia

Definition

Corneal ectasia is a progressive non-inflammatory group of disorders affecting corneal stroma with thinning and steepening that occurs pathologically or post-operatively, leading to irregular astigmatism with subsequent higher-order aberrations (HOA). This condition can be caused by iatrogenic surgery as keratoplasty and excimer laser corneal refractive surgery (Seiler et al. 1998), degenerative disease (keratoconus, pellucid marginal corneal degeneration) (Rabinowitz 1998), congenital anomaly (keratoglobus) or mechanical trauma, and injury of the cornea.

Histology

A hallmark in all ectatic diseases is stromal thinning. A recent histological study did not found any classic pathognomonic signs of keratoconus (KC), like the Bowman's layer disruption, but found the presence of thinning of collagen fibrils and decreased interfibrillar distance in the eyes with iatrogenic keratectasia (IK) (Meghpara et al. 2008). A high amount of tissue removed by the refractive procedure was associated with greater corneal biomechanical destabilization, increased corneal steepening, and a worse prognosis.

Immunohistochemical examinations revealed different expression patterns of α1-proteinase inhibitor and matrix metalloproteinases (MMP) in KC and IK eyes. KC showed lower levels of α1-proteinase inhibitor and higher levels of MMP-1 compared to normal eyes. Expression patterns in IK eyes were similar to those in normal eyes. These discrepancies suggest that KC and IK are two different entities.

Molecular Diagnostics

Recently, a few inflammatory mediators have been reported to be elevated in the tear fluid and sera of keratoconus patients (Jun et al. 2011), but there are no valid clinical molecular diagnostics available at the moment. In spite of inflammatory mediators being found in keratoconus, several issues are still to be elucidated as clinical and histological findings show little evidence of this inflammation and there is no significant cell infiltration or neovascularization, suggesting that the findings of inflammatory markers merely correspond to epiphenomena, a possibility already suggested by Lema et al. (2009).

Electron Microscopy

In keratoconus eyes, electron microscopy shows decreased thickness of the cornea with fewer lamellae. The collagen fibrils in the lamellae are thickened mildly and the space between fibrils is increased. Epithelial cells showed signs of degeneration and accumulation of ferritin (Fleischer's ring). In the stroma, a reduction of collagen lamellae and deposits beneath the keratocytes can be found. Also in Descemet's layer ruptures were found (Vogt's striae). In iatrogenic keratectasia eyes, collagen fibril thinning and decreased interfibril distance were observed in the stromal bed.

Clinical Diagnosis

There are many topography (front surface curvature), tomography (epithelial and stromal thickness profiles), and biomechanical indices published that have been used to distinguish keratoconus and ectatic corneas from normal corneas (Fontes et al. 2011). Placido disc–based corneal topography is sensitive to detect abnormal front curvature patterns of ectatic diseases in eyes with relatively normal distance-corrected visual acuity and unremarkable biomicroscopy (Ambrosio and Randleman 2013). A major application of topography is the detection and management of corneal ectasia, principally keratoconus; screening for corneal ectasia is especially important prior to refractive surgery. In the early stage, ectatic diseases are difficult to detect without a complete corneal study: topography, tomography with pachymetric map, and biomechanical parameters. Recognizing the development of ectasia early in the process is critical to maximize patient outcomes.

Differential Diagnosis

Corneal thickness profile is different in ectatic corneas so that the increase in thickness is more abrupt in these cases than in normal. Secondly, the differential diagnosis between different corneal ectatic diseases has to be made (e.g., keratoconus vs. pellucid marginal corneal degeneration).

Treatment

After corneal ectasia is established, to prevent progression, eye rubbing should be avoided. As corneal ectasia progresses and irregular astigmatism increases, many patients are no longer able to achieve satisfactory vision with spectacle correction. Corneal collagen cross-linking (CXL) may stabilize ectasia, but only indicated after progression has been documented. Visual improvement can be addressed with spectacles, rigid contact lenses, intracorneal ring segment implantation, and keratoplasty.

Cross-References

- ▶ Keratectasia
- ▶ Keratoconus
- ▶ Keratoglobus
- ▶ Pellucid Marginal Corneal Degeneration

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Ectasia, Retinal

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Synonyms

Choroidal coloboma; Chorioretinal coloboma; Fundus coloboma; Macular coloboma; Retinal coloboma; Retinochoroidal coloboma

Definition

A congenital defect, characterized by the absence of normal retina, retinal pigment epithelium, and choroid.

Etiology

Congenital ocular colobomata are caused by impaired embryogenesis. During embryogenesis, at around day 30 of gestation, the ventral surface of the optic vesicle and stalk invaginates leading to the formation of a double-layered optic cup. This invagination gives rise to the optic fissure, allowing blood vessels from the vascular mesoderm to enter the developing eye. Fusion of the edges of this fissure starts centrally around day 33 of gestation and proceeds anteriorly toward the rim of the optic cup and posteriorly along the optic stalk, with completion by 7 weeks. Failure of part of the fetal fissure to close results in the clinical entity recognized as coloboma which may affect one or more areas of the eye including the eyelid, cornea, iris, ciliary body, lens, retina, choroid, and optic nerve. Maternal exposure to alcohol and an excess amount or deficiency of vitamin A during these stages of embryonic development are risk factors. The molecular mechanisms controlling these tissue events are largely unknown although the involvement of homeobox genes such as PAX2, MSH-C, and sonic hedgehog has been described. Associations with chromosomal abnormalities or multisystem disorders, such as trisomy 13, the Aicardi syndrome, and *Goldenhar's syndrome,* have been reported (Regillo 2012).

Clinical Presentation

The extent of the defect depends on the location of the coloboma and the ocular structures involved. Incomplete or inadequate closure produces a coloboma of the iris, ciliary body, choroid, or optic disk, depending on the extent of the failed closure and secondary attempts to close the defect. When the damage is severe *microphthalmia* or *anophthalmia* may result. If the fetal fissure fails to close posteriorly, then a chorioretinal coloboma affecting the retinal pigment epithelium (RPE), neurosensory retina, or choroid may occur. The defect is essentially a bare sclera with the overlying RPE, retina, or choroid missing. In some cases, although the retina is present, it is hypoplastic and gliotic.

Usually, a chorioretinal coloboma is asymptomatic despite significant upper visual field defects as the patient is unaware of the congenital defects. Chorioretinal coloboma is usually associated with *iris coloboma* and is bilateral in more than 60% of cases. If the iris is indeed involved an inferonasal keyhole, pupil may be seen. Chorioretinal colobomata are glistening white or yellow defects, varying in size, with distinct borders that are inferior or inferonasal to the optic disk and may extend to involve the macula. The margin of the coloboma is often pigmented, and the defect can extend from the iris to the choroid and produce an inferonasal gap (Barnard 2012).

Chorioretinal colobomata increase the risk of retinal detachment, occurring in one third of cases (Schubert et al. 2005), choroidal neovascularization at its margins and cataract. Involvement of the macula, extended involvement of the retina, or refractive errors may all lead to secondary amblyopia.

Diagnosis

Physical exam may reveal congenital defects in the eyelids or iris and are typically seen after birth. Genetic counseling, when indicated, may help identify chromosomal abnormalities and systemic syndromes associated with chorioretinal coloboma (Gregory-Evans et al. 2004).

Differential Diagnosis

Ocular trauma, chorioretinal scars, *staphyloma*, and North Carolina macular dystrophy.

Prophylaxis

Avoiding alcohol intake and excess exposure or vitamin A deficiency during pregnancy is

recommended. When indicated, genetic counseling may help identify hereditary chromosomal abnormalities.

Therapy

No cure is currently available for chorioretinal coloboma. Patients with bilateral coloboma or unilateral coloboma plus one other systemic abnormality should be referred to a genetics specialist to evaluate for systemic disorders. Interval monitoring for *retinal detachment* and choroidal neovascularization should be performed with a dilated fundus exam approximately every 6–12 months or sooner if indicated. Measures such as patching should be taken to maximize visual potential of the affected side as there is often normal retina present, and refractive error is often present putting patients at risk for amblyopia. Correction of refractive error, if present, should be performed. Choroidal or retinal detachment that may occur later in life should be treated accordingly.

Monocular precautions should be strongly considered for any patient with unilateral coloboma and resulting decreased visual acuity on the affected side. Low vision (vision rehabilitation) may be of aid, if indicated.

Prognosis

The most important predictor of visual outcome is the preservation of normal foveal anatomy. However, retinal detachment, choroidal neovascularization, and cataract may further compromise the visual outcome (Olsen 1997).

Epidemiology

Most cases of chorioretinal coloboma are sporadic. The exact frequency of isolated chorioretinal coloboma is most probably underestimated as mild cases have a tendency to escape detection; however the estimated incidence is 0.2 per 10,000 live births. The most frequent type of coloboma is iris coloboma followed by combined iris and choroidal coloboma (Regillo 2012).

Cross-References

- ▶ Goldenhar Syndrome
- ▶ Iris Coloboma
- ▶ Microphthalmia
- ▶ Nanophthalmos
- ▶ Retinal Detachment
- ▶ Staphylomas, Congenital, Anterior

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Ectodermal Dysplasia

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Definition

Heterogeneous group of congenital syndromes in which ectoderm-derived tissues are altered or absent.

Overview

Ectodermal dysplasias consist of congenital abnormalities in derivatives of the surface ectoderm. Although the pathogenesis is not fully understood, many described mutations affect components of cell-to-cell communication such as ligands, receptors, or transcription factors. Resultant disruptions in cell signaling prevent in utero induction of the surface ectoderm, leading to the absence or functional impairment of adult tissues. Concordantly, ocular pathology results from the loss of superficial structures or their normal functions. Mutations are generally associated with the p63 gene.

Structure

During development the surface ectoderm is induced by neighboring mesenchyme and mesoderm to form the epidermis, hair, nails, teeth, and subcutaneous glands. It also contributes to limb formation and the branchial apparatus that forms much of the face and neck.

The formation of the eye begins with interaction between surface ectoderm and the early forebrain leading to formation of an optic cup that organizes the rest of the embryologic process (see Fig. 1). The mesoderm of the optic cup creates the choroid and sclera, while the neuroectoderm forms the retina and optic nerve. The surface ectoderm produces the ocular surface, including the corneal epithelium, bulbar and palpebral conjunctiva, meibomian glands, lacrimal glands, and nasolacrimal ducts. It also gives off a bud in early development that becomes the crystalline lens.

Function

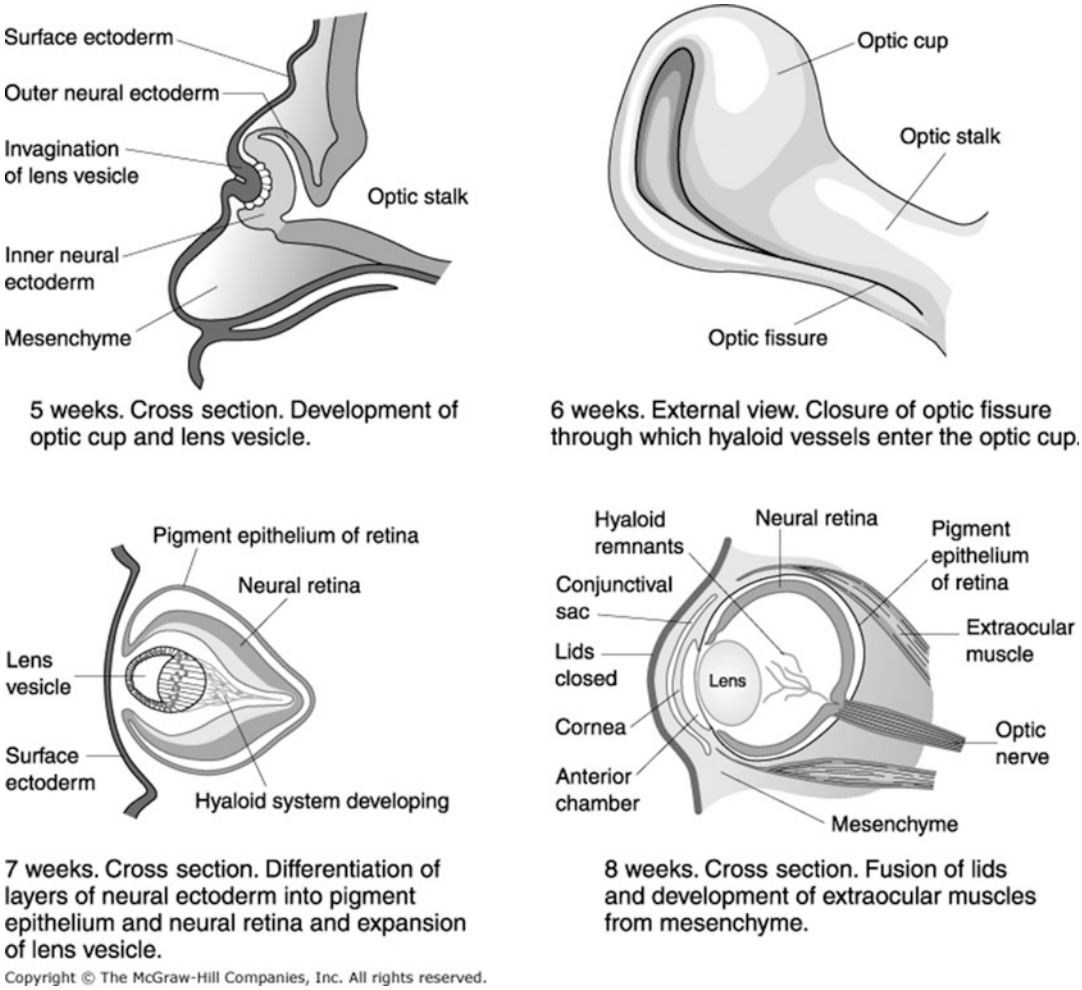
The overall role of the surface ectoderm derivatives is to form the body's protective external barrier. The epidermis prevents microbes and other pathogens from entering the body and maintains fluid and electrolyte homeostasis in cooperation with the sweat glands, which use evaporation to mediate thermoregulation. Surface ectoderm is also a precursor to hair, nails, tooth enamel, and their surrounding structures.

Like the epidermis, the corneal epithelium and bulbar and palpebral conjunctiva mediate innate immunity and act as a first barrier to the eye. The structures that form each of the three tear film layers are derived from surface ectoderm. The aqueous layer is produced by lacrimal glands and contains electrolytes and antibacterial proteins. The lipid layer is created by meibomian glands which prevent tear evaporation. The mucin layer is created by the conjunctival epithelium that creates a dispersive, hydrophilic layer. Drainage occurs via the nasolacrimal sac and duct.

Clinical Relevance

The estimated incidence of ectodermal dysplasia is 7 per 10,000 births. That number includes many syndromes with a wide array of phenotypes that can involve non-ectodermal structures. The skin, hair, teeth, and nails are the most common sources of signs and symptoms, leading to both cosmetic and functionally debilitating defects. Facial and oral defects such as anodontia or cleft lip and palate require surgical correction, as do limb abnormalities such as ectrodactyly. Genitourinary anomalies may precipitate renal failure, and mortality can occur in hyperthermia secondary to hypohidrosis.

Ocular manifestations can be progressive and particularly burdensome. Deficient tear production leads to xerophthalmia and defective drainage leads to excess tearing or epiphora. Limbal stem cell deficiency causes poor corneal epithelium which can lead to chronic epithelial defects, corneal infections, corneal scar, and, in late stages, corneal perforation. Less frequently, cases have been noted with cataracts and other ocular pathology outside the surface ectoderm such as macular degeneration.



Ectodermal Dysplasia, Fig. 1

Cross-References

- ▶ Ectrodactyly-Ectodermal Dysplasial-Clefting (EEC) Syndrome
- ▶ Meibomian Glands
- ▶ Stem Cells, Limbal, Corneal Epithelium Maintenance
- ▶ Tear Film (Tears)

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Ectopia Lentis

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Synonyms

Lens dislocation; Lens ectopy

Definition

A displacement, partial or complete, of the crystalline lens resulting from defective zonule formation. Such anatomical conditions give rise to an anterior displacement into the anterior chamber and a posterior displacement into the vitreous body.

A subluxation represents partially displaced lens still remaining within the lens space.

Etiology

Causes for a lens luxation are, for example, myopia magna with overexpansion of zonule formation, trauma (most common cause), or intraocular tumors. A possible cause is a genetical hypoplasia of zonule formation (Marfan's syndrome, Marchesani syndrome, Ehlers-Danlos syndrome, pseudoexfoliation syndrome, homocystinurie). A secondary ectopia may result from degeneration of the zonula formation by uveitis (iridocyclitis) or cataracta hypermatura.

Clinical Presentation

Symptoms of a lens displacement may become clinically apparent as diplopic images or lower visual acuity because of missed refraction of the lens (refractive myopia). If there is an anterior displacement, an acute attack of glaucoma with pain and cloudy vision is possible. An intraocular inflammation (endophthalmitis) or raising intraocular pressure can result from posterior displacement.

Diagnostics

- Visual acuity
- Slit-lamp examination
- Intraocular pressure
- Dilated fundus examination
- Echography
- Laboratory evaluation (suspicion of hereditary condition)
- If Marfan's syndrome suspected: cardiac evaluation, eyes axial length measurement
- If homocystinuria is suspected: special serum and urine examination

Differential Diagnosis

- Pseudoexfoliation
- Glaucoma
- Cataracta traumatica

Prophylaxis

In addition to regular ocular examinations, a well-timed cataract surgery for patients suffering, for example, from mature cataracts is reasonable. If the patient suffers from a currently active uveitis disease, a sufficient pharmacological therapy is important.

Therapy

An immediate surgery procedure is considered to be the only efficient therapy. The individual surgical treatment depends on the initial situation and localization of the displaced lens.

In addition to that, an anti-inflammatory treatment is indispensable.

If there is any suspicion of a general disease, a comanagement with the patient's internist or pediatrician is important.

Prognosis

The visual damage varies with the degree of lens displacement, etiologic abnormality, and age of onset.

In case of appearance of the lens dislocation during childhood, the prevention of an amblyopia is vital.

Epidemiology

The actual incidence in general population is currently unknown. In general, it can be said that the ectopia lentis is a rare clinical diagnosis. One cannot detect an age-related distribution of the affected patient, so that age cannot be ascertained as a risk factor for lens dislocation. Considering the gender distribution, the literature reports an overbalance of male patients.

Cross-References

- ▶ Cataract, Causes and Treatment
- ▶ Endophthalmitis
- ▶ Luxated Lens

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Ectopic Lacrimal Gland

▶ Choristomas

Ectrodactyly-Ectodermal Dysplasial-Clefting (EEC) Syndrome

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Synonyms

EEC syndrome; Split foot syndrome with clefting; Split hand

Definition

A combination of characteristic findings including ectrodactyly of the hands or feet, bilateral cleft lip and palate, and ectodermal dysplasia. Ectrodactyly refers to abnormal, fused, or extra fingers or toes. All abnormalities are due to dysplasia of ectodermally derived structures.

Etiology

The defects are due to mutations at a variety of possible chromosomes all affecting the p63 gene. This gene is a transcription factor active during embryogenesis that plays a role in stem cell differentiation. The mutation is usually autosomal dominant but can also be sporadic. It has variable expressivity and incomplete penetrance. Sporadic cases are usually more severe than familial cases.

Clinical Presentation

Patients present with a variety of clinical manifestations. Urogenital abnormalities include a wide spectrum of problems such as small-volume bladder, painful micturition, and recurrent infections. The skin and hair can be dry and hypopigmented. The hair can be sparse and slow growing in some patients. One of the most concerning features is a lack of sweat glands, which can lead to hyperthermia and death. The nails are often dystrophic with pitting and transverse ridges. Patients universally have many dental carries and often have secondary dentition malformations. Conductive hearing loss is often noted in patients due to missing or malformed ossicles. Ectrodactyly is often present in the upper or lower extremities. Many patients also have a bilateral cleft lip and/or palate.

The eyes are affected in several ways. The most common problem is poor functioning meibomian glands that lead to a poor lipid tear film resulting in dry eye. The second most common ocular problem is obstruction or malformation of the lacrimal drainage system. This causes excessive tearing or epiphora. With continued blockage of the tear duct, dacryocystitis, an inflammation or infection of the lacrimal sac, can occur. Both dry eye and tear stasis can cause recurring infections of both the eye and ocular adnexa. The corneal limbal stem cells constantly regenerate the corneal epithelium. Corneal scarring, ulceration, neovascularization, perforation, and progressive loss of vision are also common problems that can be attributed to corneal limbal stem cell deficiency that is common in ectodermal dysplasia. Abnormalities of the crystalline lens are not found in EEC despite its ectodermal origin.

Diagnosis

A diagnosis of EEC is made clinically. Two of the three major features are required. These include (1) some form of ectodermal dysplasia, (2) ectrodactyly, and (3) cleft lip or palate.

Differential Diagnosis

- Orofacial clefting and ectrodactyly with no signs of ectodermal dysplasia:
  - Ectrodactyly-cleft palate syndrome
- Ectodermal dysplasia and only *one* of the other major features:
  - Oligosymptomatic EEC
  - Rapp-Hodgkin syndrome
  - Ankyloblepharon ectodermal dysplasia and clefting syndrome
- Mental retardation with ectodermal dysplasia and orofacial clefting:
  - Ectodermal dysplasia, cleft palate, and mental retardation syndrome
- Ectodermal dysplasia and ectrodactyly but no orofacial clefting:
  - Lacrimo-auricular-dento-digital syndrome

Prophylaxis

Genetic screening and meeting with a genetic counselor is recommended to discuss the 50% possibility of passing the mutation on to future generations.

Therapy

Therapy for EEC involves a plastic surgeon repairing dysplastic features such as a cleft lip or palate and dysplastic hands and feet. A renal ultrasound should be recommended to look for any urogenital malformations, and extensive dental work may be needed. If hypohidrosis is present, it is important to educate the patient and family on methods to regulate body temperature and to avoid long periods of heat exposure.

Ophthalmic treatment goals should be focused on protecting the eyes and preserving vision. Most patient's ocular manifestations involve the ocular surface. Artificial tears and surface lubrication, both lipid and aqueous based, can be used for dry eye. For patients with poor drainage and excessive tears a dacryocystorhinostomy (DCR) can be performed. These patients are also susceptible to ophthalmic infections and should be

monitored closely. If an infection is diagnosed, topical antibiotic drops are effective for ocular infections, and systemic antibiotics drops are needed for ocular adnexal infections. Supportive ocular surface care with soft contact lenses, artificial tears, or mild steroids is beneficial to prevent corneal scarring and vision loss. Corneal transplants have a better prognosis if most of the corneal limbal stem cells are intact. If there is significant loss of corneal limbal stem cells and poor corneal epithelium, a combined cadaveric limbal stem cell transplant and corneal transplant, or keratoprosthesis may be the only option.

Prognosis

Progressive loss of vision and overheating causes the greatest morbidity. Hyperthermia due to the absence of sweat glands can lead to seizures, coma, and death. Patients with EEC rarely have intellectual disabilities and can be expected to live a full and productive life with close management.

Epidemiology

Rare, but the true prevalence is unknown. There is no correlation with race, sex, or socioeconomic status.

Cross-References

► Corneal Ulcers
► Ectodermal Dysplasia

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Eczema

► Dermatitis

Eczema, of Eyelid

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Definition

Eczema of the eyelid is a dermatitis of the eyelid. It results in mild to severe itching and redness that is caused by allergies, reactions to an irritant, or atopic dermatitis.

Cross-References

► Atopic Dermatitis

Edema, Eyelid

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Definition

Eyelid edema is swelling of the eyelids that can result from a variety of causes.

Etiology

Periorbital edema most commonly occurs from allergy, angioedema, or localized lymphedema. Eyelid edema may be caused by both local and systemic conditions.

Classification/Occurrence

Local inflammatory diseases may cause eyelid edema. Contact dermatitis is one of the most common causes of cutaneous eyelid inflammation and is due to allergy or irritation from exposure to chemicals via direct application or contamination from the fingers and hands. Angioedema is an abrupt, usually bilateral, deep dermal swelling mediated by a type I allergic reaction. In addition, rosacea, allergy, or insect bites may also cause eyelid edema.

Local infections such as bacterial (blepharitis, hordeolum, chalazion), viral (herpes simplex, herpes zoster), and parasitic or protozoal infections (trichiniasis, filariasis, onchocerciasis, trypanosomiasis, and malaria) can cause eyelid edema. Preseptal or orbital cellulitis as well as intraocular infections may also cause periorbital edema.

In addition, eyelid edema may be a reflection of systemic disease including hypoalbuminemia, renal disease, and congestive heart failure causing bilateral, boggy, nontender, nondiscolored soft-tissue swelling. In addition, myxedema, dermatomyositis, lymphoproliferative disease, superior vena cava syndrome, drug eruption, and certain collagen vascular diseases may be associated with eyelid edema. Generalized or regional edema as well as other signs and symptoms consistent with each respective disease should also be present.

Other causes include blunt trauma, where a history of trauma is present, and eyelid swelling is self-limited. Tumors that involve the eye may rarely cause eyelid edema including hemangiomas of the lid as well as certain ocular or orbital neoplasms. In addition, lymphedema may be present after the lymphatic drainage system from the eyelid is interrupted.

Cross-References

▶ Eyelid Erythema

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Edinger-Westphal Complex

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Synonyms

Edinger-Westphal Nucleus

Definition

The Edinger-Westphal complex, also known as the Edinger-Westphal nuclei (EWN), is a group of neuron cell bodies that lie under the aqueduct

of Sylvius in the midbrain, just posterior to the oculomotor motor nuclei (of cranial nerve III) in the midbrain. Each EWN receives bilateral input from interneurons of the pretectal area (olivary pretectal nucleus) via the posterior commissure, which in turn receive afferent input from light-sensitive W-type ganglion cells of the retina whose axons run in the optic nerve (cranial nerve II). The EWN serves as the site of origin for cholinergic preganglionic parasympathetic fibers that run along the oculomotor nerve (cranial nerve III) and synapse in the ciliary ganglion in the orbit. From the ciliary ganglion, postsynaptic parasympathetic fibers run with the short ciliary nerves to provide motor innervation to the smooth muscle of the iris pupillary sphincter, leading to pupillary constriction in response to light (the pupillary light reflex). Pupillary constriction also occurs when looking at a near object along with convergence and accommodation (i.e., the near synkinesis reflex). This pathway involves fibers from the nucleus of Perlia (of the occipitomesencephalic tract) that synapse in the EWN and eventually make their way to the ciliary muscle to increase lens thickness and refractive power for focusing on a near object.

Cross-References

- ▶ Accommodation, Cataract
- ▶ Ciliary Ganglion
- ▶ Cranial Nerve III (Oculomotor Nerve)
- ▶ Oculomotor Nerve
- ▶ Pupillary Block
- ▶ Pupillary Light Reflex

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Edinger-Westphal Nucleus

▶ Edinger-Westphal Complex

EDS I: Classic Type, Gravis Type

▶ Ehlers-Danlos Syndrome, Gene Linkage of Disease

EDS II: Mild Classic Type, Mitis Type

▶ Ehlers-Danlos Syndrome, Gene Linkage of Disease

EDS IV: Vascular Type, Arterial Type, Ecchymotic Type, Sack-Barabas Type

▶ Ehlers-Danlos Syndrome, Gene Linkage of Disease

EDS VI: Kyphoscoliotic Type, Ocular-Scoliotic Type, Nevo Syndrome, Brittle Cornea Syndrome (Variant of Ehlers-Danlos Type VI)

▶ Ehlers-Danlos Syndrome, Gene Linkage of Disease

EDTA Chelation Therapy

▶ Chelation Therapy, for Calcific Band Keratopathy

EEC Syndrome

▶ Ectrodactyly-Ectodermal Dysplasial-Clefting (EEC) Syndrome

Efferent Visual System (Ocular Motor Pathways)

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Definition

The efferent visual system is composed of the ocular motor pathways ("infranuclear" pathways) that originate from cranial nerve nuclei III, IV, and VI of the midbrain and brainstem. These three cranial nerves control the extraocular muscles of the eye. Internuclear pathways (e.g., medial longitudinal fasciculus) coordinate ocular motor nuclei activity along with the infranuclear pathways to produce conjugate eye movements (matched rotation of the eyes in the orbit to stabilize the visual world) such as vertical and horizontal saccades (rapid relocation of gaze fixation), smooth pursuit (slow, involuntary following of moving target), vestibular movements (initiated by input from semicircular canals responding to head movement), and convergence (involved in depth perception and near synkinesis). This system works with the afferent visual system to keep the target of visual fixation on the macula (area of retina responsible for high-acuity vision).

Cranial Nerve III: Oculomotor Nerve

The nuclei of the oculomotor nerves lie in the midbrain at the level of the superior colliculus, ventral to the cerebral aqueduct and periaqueductal gray. The oculomotor nerve provides ipsilateral motor innervation to most of the extraocular muscles of the eye except the superior oblique (innervated by CN IV) and lateral rectus muscles (innervated by CN VI). The extraocular muscles innervated by CN III are the inferior oblique, medial rectus, superior rectus, and inferior rectus. A CN III palsy results in a "down and out" position of the eye due to loss of function of all muscles except the superior oblique and lateral rectus muscles, controlled by the trochlear and abducens nerves, respectively.

Cranial Nerve IV: Trochlear Nerve

The trochlear nerve nucleus provides contralateral motor innervation to the superior oblique muscle, which abducts, depresses, and internally rotates (intents) the eye. The trochlear nucleus is also located in the midbrain, caudally to the oculomotor nucleus at the level of the inferior colliculus.

Cranial Nerve VI: Abducens Nerve

The abducens nerve provides motor innervation to the ipsilateral lateral rectus muscle that produces abduction. The abducens nucleus, located in the caudal pons, is also critically involved in horizontal conjugate movements of the eye. When activated by the paramedian pontine reticular formation (PPRF), the nucleus not only activates the ipsilateral lateral rectus muscle via the abducens nerve but also sends excitatory projections via the medial longitudinal fasciculus (MLF) to the contralateral oculomotor nucleus that controls the medial rectus muscle. In this way, the abducens nucleus is the final common pathway

for the control of voluntary and involuntary horizontal conjugate eye movements.

Cross-References

- ▶ Cranial Nerve III (Oculomotor Nerve)
- ▶ Cranial Nerve IV (Trochlear Nerve), CNIV
- ▶ Cranial Nerve VI (Abducens Nerve)
- ▶ Paramedian Pontine Reticular Formation and Abducens Nucleus

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Ehlers-Danlos Syndrome, Angioid Streaks in

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Synonyms

Angioid streaks – Ehlers-Danlos syndromes

Introduction

Ehlers-Danlos syndromes (EDS) comprise a heterogeneous group of diseases of the connective tissue. The features of EDS were first described by Hippocrates in 400 BC. The syndrome is named after two physicians, Edvard Ehlers from Denmark and Henri-Alexandre Danlos from France, who described it at the turn of the twentieth century (Parapia and Jackson 2008; Georgalas et al. 2009).

EDS is caused by a defect in the structure, production, or processing of collagen or proteins that interact with collagen. This disease is characterized by fragility of the soft connective tissues and widespread manifestations in the skin, ligaments, joints, blood vessels, and internal organs. The clinical spectrum varies from mild skin and joint hyperlaxity to severe physical disability and life-threatening vascular complications. The overall incidence is 1 in 5,000 births, with higher rate among blacks. There is no cure yet for EDS, and treatment is supportive (Georgalas et al. 2009; Ryan et al. 2013).

Among these patients it is common to find angioid streaks on ophthalmologic examination.

Definition

Angioid streaks were initially described in 1889 by Doyne. They were described as irregular radial lines spreading from the optic nerve to the retinal periphery in a patient with retinal hemorrhages due to blunt trauma. Knapp was the first to use the term "angioid streaks" since the funduscopic appearance of the lines was similar to that of blood vessels. In 1917 Kofler correctly determined that angioid streaks represented changes at the level of Bruch's membrane (Parapia and Jackson 2008).

Histopathologic studies have demonstrated that angioid streaks represent irregular dehiscence in the thickened and calcified Bruch's membrane (Georgalas et al. 2009).

Systemic Conditions Associated with Angioid Streaks

Associations have been found between angioid streaks and systemic conditions such as pseudoxanthoma elasticum (Gronblad-Strandberg syndrome), Paget's disease, sickle cell anemia, acromegaly, and fibrodysplasia hyperelastica (Ehlers-Danlos syndrome). However angioid streaks may also occur in patients without associated systemic disease (Parapia and Jackson 2008; Georgalas et al. 2009; Ryan et al. 2013).

Etiology

Klein proposed a dual mechanism for the development of Bruch's membrane angioid streaks including a primary abnormality in the fibers of Bruch's membrane and increased deposits of metal salts or an increasing tendency for their pathologic deposition (Parapia and Jackson 2008; Georgalas et al. 2009).

The deposition of calcium may cause Bruch's membrane to become more brittle and increases the likelihood of developing choroidal rupture.

Furthermore it has been shown that tissue metalloproteinase, specifically MMP-9 which is known to induce basement membrane destruction and angiogenesis, was found in higher concentrations in the excised Bruch's membrane in areas of choroidal neovascularization in some eyes with angioid streaks (Georgalas et al. 2009; Ryan et al. 2013; Schubert 2014–2015).

In the early stages, angioid streaks consist of partial breaks of the calcified Bruch's membrane with thinning of the RPE, without any significant anatomic changes in the overlying retinal layers. In advanced stages, a full-thickness break of Bruch's membrane may occur followed by atrophy of the choriocapillaris, RPE, and photoreceptors. Fibrovascular proliferation from the choroid may occur through the Bruch's membrane break resulting in choroidal neovascularization and subsequent development of a disciform scar (Parapia and Jackson 2008; Georgalas et al. 2009; Ryan et al. 2013; Schubert 2014–2015).

Clinical Presentation

Angioid streaks usually originate adjacent to the optic nerve and may either radiate out or surround it concentrically and appear as irregular lines of varying width. The subretinal lines can range in diameter from 50 to 500 μm. The color of angioid streaks varies and depends on fundus pigmentation and the degree of the atrophy of the overlying RPE. Thus, angioid streaks are reddish in light-colored individuals, while in patients who have darker background pigmentation, they are usually medium to dark brown (Georgalas et al. 2009; Schubert 2014–2015).

Angioid streaks remain unchanged or may increase in length and width over time. There are no clinical studies determining the rate of their propagation in correlation with time. New streaks may be formed adjacent to old lesions and adjacent RPE and choriocapillaris may develop atrophy (Parapia and Jackson 2008).

Additional fundus findings in this condition include optic disc drusen, peripheral round atrophic scars, and a lighter orange appearance against the darker orange color of the normal RPE and choroid. At the interface between the abnormal light color and the normal darker color, the fundus has a fine, stippled appearance referred to as peau d'orange ("the skin of an orange"). Small, round retinal pigmented dots, known as crystalline dots, are also frequently present in the mid-peripheral retina (Parapia and Jackson 2008; Georgalas et al. 2009; Ryan et al. 2013).

Usually patients remain asymptomatic, and angioid streaks are an incidental finding during a routine ophthalmological investigation, unless the macula is involved with the development of traumatic rupture of the Bruch's membrane or choroidal neovascularization.

In cases with macular involvement, patients usually report metamorphopsia, blurred vision, or decreased central vision (Parapia and Jackson 2008).

Rupture of Bruch's membrane in cases of blunt head or ocular trauma may be followed by subretinal hemorrhages. It has been reported that up to 15% of patients with angioid streaks develop significant visual loss after mild head injury (Parapia and Jackson 2008; Georgalas et al. 2009).

The most common significant complication of angioid streaks is the development of choroidal neovascularization CNV, which is often bilateral, and the incidence varies between 72% and 86% in numerous studies. CNV usually is asymmetric with a mean interval of 18 months between the development of CNV in the first and fellow eye.

The risk of developing CNV increases with age. The wider and longer are the angioid streaks

the higher the risk for CNV and especially if the lesions are located in a distance less than one optic disc diameter from the fovea (Parapia and Jackson 2008; Georgalas et al. 2009; Ryan et al. 2013).

The standard outcome is poor if CNV in the macular region remains untreated because it leads to further extensive formation of subfoveal scarring causing severe loss of visual acuity. More than 50% of such patients eventually become legally blind with very poor visual acuity.

Diagnosis

Usually the diagnosis of angioid streaks is made on funduscopic examination, but ophthalmological imaging, in particular fluorescein angiography (FA), may be helpful in detecting angioid streaks and associated choroidal neovascularization when the findings are subtle (Parapia and Jackson 2008; Ryan et al. 2013; Schubert 2014–2015).

Fluorescein Angiography (FA)

FA demonstrates irregular hyperfluorescence of the angioid streaks during the early phase followed by varying degrees of staining during late phases. In some individuals with deeply pigmented choroidal tissue, the angioid streaks may be difficult to detect angiographically, whereas in light-pigmented individuals, fluorescein angiography may aid in the identification of the angioid streaks prior to their clinical detection. Fluorescein leakage is evident when CNV is present (Parapia and Jackson 2008; Georgalas et al. 2009).

Fundus Autofluorescence (FAF)

FAF imaging uses light emission from lipofuscin in RPE cells and is considered to reflect RPE metabolic activity. Fundus autofluorescence often demonstrates hypo-autofluorescence representing RPE atrophy, which can be seen more extensively than that seen on fundus ophthalmoscopy or FA. It is a useful noninvasive tool to monitor the progression of the RPE damage and choroidal neovascularization (Parapia and Jackson 2008; Georgalas et al. 2009; Schubert 2014–2015).

Indocyanine Green Angiography (ICGA)

ICGA is useful among patients with some scarring that may obscure the presence of active CNV. In these cases ICG angiography demonstrates the neovascularization more clearly than fluorescein angiography. It shows the hyperfluorescent lines with "pinpoints" in brighter areas of hyperfluorescence that are enhanced through the late stages suggesting the presence of CNV.

Spectral Domain Optical Coherence Tomography (SD OCT)

SD OCT has been shown to be helpful in detecting abnormalities in Bruch's membrane as well as the presence of subretinal fibrosis and deposits that can be difficult to demonstrate on FAF, FA, or ICGA (Parapia and Jackson 2008; Georgalas et al. 2009).

Treatment

There is no known prophylactic treatment for the formation of angioid streaks. The use of safety glasses may be advised for patients with angioid streaks because their eyes are particularly susceptible to choroidal rupture even after minor blunt injury. Treatment strategies are only directed to treat eyes with choroidal neovascularization, since untreated CNV results in poor visual outcomes.

Laser Photocoagulation

In the past prophylactic therapy of angioid streaks with thermal laser in order to prevent CNV development has failed and in some cases even induced CNV formation. Some studies have shown that

laser treatment for extrafoveal CNV related to angioid streaks resulted in better visual outcome than untreated eyes. On the other hand, results of photocoagulation for the treatment of foveal CNV demonstrate a high recurrence rate of up to 77% and poor overall visual outcomes (Parapia and Jackson 2008; Georgalas et al. 2009).

Transpupillary Thermotherapy (TTT)

TTT employs diode laser beam of 810 nm wavelength, with a lower threshold to avoid producing a thermal burn. This treatment has a better penetration to the choriocapillaris and is less damaging to the RPE. However a retrospective study investigating the use of TTT in treatment of subfoveal choroidal neovascularization found no significant long-term benefit in reducing the growth of the CNV or in visual improvement.

Photodynamic Therapy (PDT)

Data from both retrospective and prospective case series of eyes treated with PDT demonstrate variability and contradictory results on visual outcomes (Georgalas et al. 2009; Schubert 2014–2015).

In conclusion, from all previous studies and case reports, it is evident that despite the initial encouraging results from the application of PDT for the treatment of foveal CNV, the end results did not fulfill the initial expectations. However some may consider PDT as an adjuvant therapy that does not prevent, but slows down the natural course of CNV.

Macular Translocation

This surgical technique was introduced by Machemer and Steinhorst in 1993, which was applicable prior to the use of anti-vascular endothelial growth factor (VEGF) treatments for CNV.

This surgical technique involves moving the macular neuroretina to lie on top of an area of RPE without previous CNV. Several techniques have been described including a limited translocation as well as a 360° translocation where the entire retina is rotated. However, this is a complex, difficult, long-lasting operation with serious complications which can threaten the patient's vision.

In the few studies that employed this technique, varying short-term visual acuity improvement has been reported, but one should keep in mind that the number of eyes treated was limited.

Anti-VEGF Treatment

Laser photocoagulation, TTT, and PDT have not been as successful in reducing the degree of visual loss compared with the visual outcomes following anti-VEGF therapy. Treatments with anti-VEGF therapies such as bevacizumab or ranibizumab have demonstrated a marked reduction in the incidence of severe visual acuity loss in the treated eyes compared to the untreated eyes, though follow-up is short and randomized trials are lacking.

Further investigations involving combination therapy are needed before determining its added benefit over monotherapy with anti-VEGF treatment alone (Parapia and Jackson 2008; Georgalas et al. 2009).

Prognosis

As described above, patients with angioid streaks usually are asymptomatic unless complications such as macular choroidal neovascularization develop. In case of macular involvement, the prognosis is often poor, with higher than 50% of eyes progressing to legal blindness without treatment (Georgalas et al. 2009; Ryan et al. 2013; Schubert 2014–2015).

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Ehlers-Danlos Syndrome, Gene Linkage of Disease

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Synonyms

EDS I: classic type, gravis type; EDS II: mild classic type, mitis type; EDS IV: vascular type, arterial type, ecchymotic type, Sack-Barabas type; EDS VI: kyphoscoliotic type, ocular-scoliotic type, Nevo Syndrome, Brittle Cornea Syndrome (variant of Ehlers-Danlos Type VI)

Definition

Ehlers-Danlos syndrome (EDS) is a rare, inherited disorder caused by defective collagen synthesis. It is part of a large heterogeneous group of connective tissue disorders characterized by skin and joint hyperextensibility and easy bruisability with poor scar formation. Over 10 distinct clinical subtypes exist based on biochemical, genetic, and clinical variations; those subtypes with ocular manifestations are included in Table 1, below (Lorenz and Moore 2006; Kanski and Bowling 2011; Krachmer et al. 2011; Chaudhuri and Vanathi 2012; Goldman and Schafer 2012).

Etiology

All forms of EDS result from defective synthesis and metabolism of elastin, proteoglycans, and

Ehlers-Danlos Syndrome, Gene Linkage of Disease, Table 1 A summary of Ehlers-Danlos Syndrome classifications and associated gene linkage

Type	Prevalence	Systemic findings	Ocular manifestations	Gene linkage
EDS type I	1 in 20,000	EDS type I is the most common severe form. The skin is easily hyperextensible and bruisable.	Epicanthal folds are a common finding. Eyelids can be easily stretched and everted. Retinal detachment has also been reported.	*COL5A1* (9q34.3), *COL5A2* (2q32.2) or *COL1A1* (17q21.33).
EDS type II	1 in 20,000	EDS type II resembles type I but has milder clinical findings and is hence called the "mitis" type. It has similar prevalence as EDS type I.	Epicanthal folds are a common finding.	*COL5A1* (9q34.3) or *COL5A2* (2q32.2).
EDS type IV	1 in 200,000	EDS type IV is related to abnormalities in medium-sized arterial vessels.	Ocular complications involve carotid-cavernous fistulas giving rise to ocular bruits, proptosis, conjunctival hyperemia and chemosis, blurred vision, diplopia, and orbital pain. Further perfusion compromise can cause ocular ischemia.	*COL3A1* (2q32.2)
EDS type VI	1 in 100,000	EDS type VI is characterized by severe kyphoscoliosis, generalized joint laxity, and skin involvement.	Globe rupture and rhegmatogenous retinal detachment may occur as a result of minor trauma or spontaneously. Other ocular manifestations in EDS type VI include myopia, thin, blue sclerae, and microcornea with normal intraocular pressure. These features make this subtype of most interest to ophthalmologists.	*PLOD1* (1p36.22)

macromolecular proteins in the extracellular matrix of various tissues, the most abundant of which is collagen. In majority of EDS cases, mutations in a wide variety of genes cause altered structure, synthesis, posttranslational modifications, or stability of involved collagen molecules. This leads to decreased synthesis of collagen, defective collagen fibril crosslinking, or decreased function of involved collagen-processing enzymes, such as lysyl hydroxylase 1 in EDS type VI.

EDS type I is caused by an autosomal dominant mutation in collagen alpha-1(V) (*COL5A1* [9q34.3]), collagen alpha-2(V) (*COL5A2* [2q32.2]), or rarely in collagen alpha-1(I) (*COL1A1* [17q21.33]) genes. These genes code for the alpha chain in type V and type I collagen. The mutations result in defective production of type V and type I collagen. EDS type II is caused by an autosomal dominant mutation in collagen alpha-1(V) (*COL5A1* [9q34.3]) or collagen alpha-2(V) (*COL5A2* [2q32.2]) genes only.

EDS type IV is caused by an autosomal dominant, or rarely autosomal recessive, heterozygous mutation in the type III collagen gene (*COL3A1* [2q32.2]). This mutation causes structural defects in pro-alpha-chains of type III procollagen.

EDS type VI is caused by an autosomal recessive homozygous or compound heterozygous mutation in the *PLOD1* (1p36.22). This gene codes for lysyl hydroxylase 1 – an enzyme responsible for the formation of hydroxylysyl groups in collagen molecules. These groups become important attachment sites for carbohydrates in collagen molecules. The *PLOD1* mutation results in reduced stability of collagen intermolecular crosslinking (Lorenz and Moore 2006; Kanski and Bowling 2011; Krachmer et al. 2011; Chaudhuri and Vanathi 2012; Goldman and Schafer 2012).

Clinical Presentation

Patients with EDS may present with dry eyes, steep corneas, pathologic myopia, and abnormal vitreous. Epicanthal folds are identified with classical EDS type I and II. Keratoglobus is associated with EDS type VI.

An association between EDS and ectopia lens has been reported; collagen type IV is present in zonular fibers but the molecular mechanisms underlying such weakness are unclear and may be related to myopic change.

In EDS type VI, a variant also known as brittle cornea syndrome, patients demonstrate a biochemical defect other than lysyl hydroxylase. Associated with keratoglobus or keratoconus, minor trauma may cause rupture of the globe with risk of retinal detachment due to increased corneal and scleral fragility and thinning. Corneas with significant anterior bulging may experience Descemet membrane detachment, resulting in the appearance of a thin cornea with corneal haze. A thin sclera appears blue due to relatively increased transparency and visualization of underlying uvea.

Systemically, characteristic findings are hypermobile joints and hyperextensible skin. Cardiovascular disease involves bleeding diathesis, dissecting aneurysms, spontaneous rupture of large blood vessels, and mitral valve prolapse. Other systemic features include kyphoscoliosis, diaphragmatic hernia, carotid-cavernous fistula, and diverticula of the gastrointestinal and respiratory tracts (Lorenz and Moore 2006; Kanski and Bowling 2011; Krachmer et al. 2011; Chaudhuri and Vanathi 2012; Goldman and Schafer 2012).

Diagnosis

Diagnosis of the different subtypes of EDS is based on careful evaluation of clinical features and use of laboratory tests. Classical type EDS (type I and II) is diagnosed based on clinical examination. Diagnosis of EDS type IV (vascular type) may be more definitively confirmed by genetic testing for mutations in *COL3A1* or a skin biopsy indicating collagen changes in cultured fibroblasts. Urinary enzyme assay can help establish the diagnosis of EDS type VI (kyphoscoliotic type) (Lorenz and Moore 2006; Kanski and Bowling 2011; Krachmer et al. 2011; Chaudhuri and Vanathi 2012; Goldman and Schafer 2012).

Differential Diagnosis

Other non-EDS disorders with similar clinical presentation should be considered and excluded in the patient workup. Marfan syndrome may present with infantile kyphoscioliosis also seen in EDS type VI. Larsen's syndrome resembles the arthrochalasis type of EDS due to similar joint hypermobility. Cutix laxa may resemble the skin involvement and loss of elasticity in dermatosparaxis type of EDS (Lorenz and Moore 2006; Kanski and Bowling 2011; Krachmer et al. 2011; Chaudhuri and Vanathi 2012; Goldman and Schafer 2012).

Prophylaxis

Genetic counseling should be given to all patients on mode of inheritance and risk of having children with EDS. Prenatal diagnosis of all EDS types with specific molecular defects may be a useful screening tool. Biochemical and genetic screening may elucidate defects in type III collagen in relatives at risk. Patients with vascular EDS should be advised to avoid contact sports and to manage high blood pressure. Arteriography and arterial lines should also be avoided (Lorenz and Moore 2006; Kanski and Bowling 2011; Krachmer et al. 2011; Chaudhuri and Vanathi 2012; Goldman and Schafer 2012).

Therapy

Correct diagnosis of EDS and specific subtype should be established if possible before appropriate management plan is formulated. The kyphoscoliotic type of EDS may improve with administration of vitamin C by compensating for enzyme deficiencies; no metabolic or genetic therapy is effective in other forms of EDS.

Management of ocular manifestations is challenging due to poor wound healing or approximation. In EDS type VI, in particular, management of spontaneous globe rupture necessitates a careful surgical approach due to corneoscleral fragility; epikeratoplasty allows addition of donor corneal tissue for stability while preserving host cornea, although reports are few (Lorenz and Moore 2006; Kanski and Bowling 2011; Krachmer et al. 2011; Chaudhuri and Vanathi 2012; Goldman and Schafer 2012).

Prognosis

Life expectancy is comparable to the general population except for patients with EDS type IV, in which it is decreased to approximately 50 years of age (Lorenz and Moore 2006; Kanski and Bowling 2011; Krachmer et al. 2011; Chaudhuri and Vanathi 2012; Goldman and Schafer 2012).

Epidemiology

Incidence of EDS has been estimated to be about 1 in 5000 births and worldwide prevalence to be about 1.5 million people (Lorenz and Moore 2006; Kanski and Bowling 2011; Krachmer et al. 2011; Chaudhuri and Vanathi 2012; Goldman and Schafer 2012).

Cross-References

- ▶ Blue Sclera
- ▶ Keratoglobus Basic Science

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Elastoid Degeneration

▶ Keratinoid (Spheroidal) Degeneration
▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
▶ Spheroidal Degeneration

Elastotic Degeneration

▶ Keratinoid (Spheroidal) Degeneration
▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
▶ Spheroidal Degeneration

Electrical Evoked Response (EER)

▶ Electrically Evoked Potentials

Electrical Response of the Retina to a Light Stimulus, The

▶ Electroretinogram

Electrically Evoked Potentials

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Synonyms

Electrical Evoked Response (EER); Phosphene

Definition

The electrically evoked potential (EEP) is the electrical activity in the visual cortex (V1) that is triggered by trans-corneal electrical stimulation. The psychophysical description of visual perception, reported by subjects who undergo electrical stimulation of the globe, is called phosphene.

This is in distinction from electrical activity in the visual cortex that is generated in response to light stimuli (visually evoked potential, VEP).

Purpose

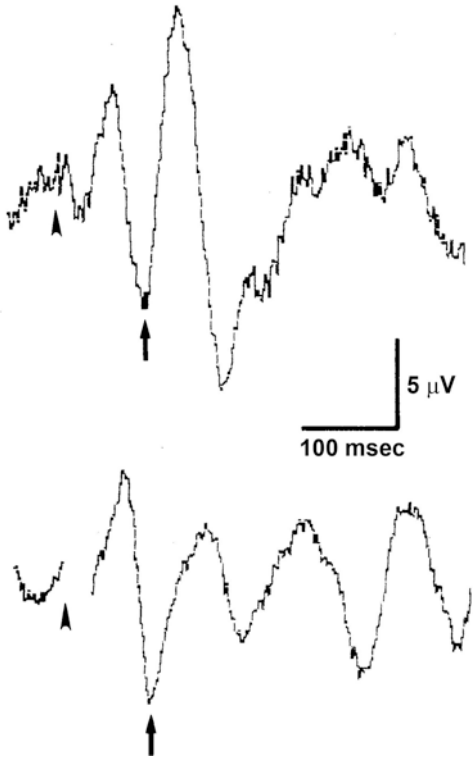
The electrically evoked potential (EEP) is used to assess the functional integrity of the visual nervous system, including the retinal ganglion cells, optic nerves, visual pathways, and primary visual cortex (V1) in cases where simple visual stimuli cannot be used (Dorfman et al. 1987).

Principle

The visual system, like any other sensory modality, depends upon electrical activity that is generated in the receptors (hair cells in the ear, photoreceptors in the retina) in response to a physical stimulus (sound, light). The information conveyed to the appropriate region in the brain from any physical stimulus is a pattern of electrical activity, which is further processed in the brain leading eventually to perception. Therefore, any pattern of electrical activity transmitted from the eyes to the primary visual cortex (V1) regardless of its physical source is perceived as light.

Electrical activity in the visual pathways that is elicited by stimuli other than light, such as physical pressure or by electrical stimulation, will all be interpreted in the brain as reflecting light stimuli, which are called phosphenes.

The electrically evoked potential (EEP) is elicited by trans-corneal electrical excitation while recording electrical activity from the visual cortex using scalp electrodes placed over the occipital lobe in a pattern similar to that used to record the visually evoked potential (VEP). Trans-



Electrically Evoked Potentials, Fig. 1 Electrical evoked potential and visual evoked potential, obtained by stimulating the same eye in a healthy volunteer, are compared. Timing of stimuli is marked by an arrowhead and the preeminent negative wave by an arrow.

corneal electrical excitation can be achieved with a bipolar corneal electrode or by a monopolar electrode placed on the cornea, while the ground electrode is placed either on the forehead or the temporal skin. The cornea needs to be anesthetized in order to prevent any discomfort to the patient (Potts et al. 1968; Gekeler et al. 2006).

Figure 1 compares visually evoked potential (VEP) elicited by flashlight stimuli to electrically evoked potential (EEP) that was elicited by square 5-ms pulses of 500 μA applied to the cornea using a bipolar corneal electrode. The VEP and EEP were recorded by stimulating the same eye. Recording from the visual cortex was done using a bipolar recording configuration. The active electrode was placed along the midline about 3 cm above the inion, the reference electrode was placed 5 cm further up along the midline, and an ear-clip served as ground electrode. The small gap in the trace of the EEP is the photoelectric artifact. Arrowheads denote timing of stimuli, and arrows point to the first negative wave. The pattern of the VEP and EEP differ; the EEP is composed of several consecutive waves, while the VEP is more robust and is composed of a negative wave followed by a positive wave.

Indication

The electrically evoked potential (EEP) was suggested for the following:

1. Very opaque optical media: in cases when bright light stimuli are not sufficient to test potential visual function, the EEP can be used to assess the functional integrity of the visual pathways from the eyes through the lateral geniculate nuclei and to the primary visual cortex (V1).
2. Candidates for implantation of retinal neuroprosthesis: Electrical neuroprosthetic devices have been developed and approved for clinical use in blind patients suffering from advanced retinitis pigmentosa. Evaluation of the integrity of the visual nervous pathways before surgical implantation of the prosthesis is imperative for assessment of the potential for visual restoration. A bright flash VEP and ERG can be used but in very advanced cases of retinitis pigmentosa, even intensely bright flashes may not elicit a measurable cortical response. In these cases, trans-corneal electrical stimulation can be used to check for detection of phosphenes or more objectively for recording the EEP to indicate whether electrical stimulation can elicit brain activity.

Contraindication

Severe damage to the cornea.

Advantage/Disadvantage

Advantage: test optic nerve function, bypassing photoreceptors.

Disadvantage: not clear which retinal elements are stimulated, may be moderately uncomfortable.

Cross-References

- ▶ Cornea
- ▶ Prosthesis
- ▶ Retinitis

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Electrocautery

- ▶ Thermal Cautery

Electromagnetic Energy/Radiation, Adverse Effects on Retina

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Synonyms

Light-induced retinal damage; Phototoxicity

Definition

Electromagnetic radiation is any form of energy generated by electromagnetic process, ranging between x-rays to microwaves. The visible range of electromagnetic radiation is characterized by wavelength spectrum that spans from 400 nm (purple blue) to 700 nm (red). Whereas light in the visible range is essential for physiological visual function, exposure to excessive electromagnetic energy of any wavelength can result in tissue damage to the retina through one of several general mechanisms, including photochemical, thermal, or mechanical injury. The particular mechanism activated depends on the wavelength, duration of exposure, and energy of electromagnetic radiation.

1. Photochemical damage: reflects excessive activation of the phototransduction cascade in the rod photoreceptors leading to apoptosis of the retinal pigment epithelial (RPE) cells and photoreceptors. Photochemical retinal damage, first described in albino rats, depends upon light intensity, its color, duration of light exposure, body temperature of animal, and other parameters and is characterized by irreversible reduction in the ERG amplitudes associated with degeneration and loss of photoreceptors and RPE cells. The pathological mechanism of this photochemical injury is yet to be elucidated, but several hypotheses have been speculated, including light-induced oxidative stress and metabolic stress.

   To date, no clinical correlate of this kind of retinal injury has been described in humans.
2. Thermal damage: occurs when light is absorbed by non-visual pigments in the retina such as melanin, hemoglobin, or lipofuscin and causes local temperature rise and thermal stress to the tissue. The local heat response can result in denaturation of proteins, loss of tertiary structure of proteins and macromolecules, and loss of membrane structure. Higher energy levels can cause photocoagulation of tissue.

   In clinical ophthalmology, the principle of controlled photothermal retinal damage is commonly applied for the treatment of retinal conditions including laser retinopexy around

retinal breaks or laser photocoagulation for leaking blood vessels.

3. Mechanical damage: occurs when excessive energy from electromagnetic radiation generates tensile forces in the tissue, leading to formation of cavitation and structural tissue disruption.

In ophthalmology, pulsed lasers that produce photodisruption of tissue are used for producing precise holes or cuts, particularly in the anterior segment. For example, the pulsed Nd:YAG laser is commonly used to perform capsulotomy when visually significant opacification of the posterior lens capsule occurs after surgical cataract extraction. However, pulsed lasers can be lethal to the RPE and carry a high risk of collateral damage to the retina and therefore are rarely employed for procedures of the posterior segment.

Cross-References

- ▶ Capsulotomy
- ▶ Neodymium:Yag Laser

Electromagnetic Spectrum

- ▶ Frequency of Light Wave

Electrooculogram

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Synonyms

Arden ratio; Standing potential of the eye; The corneo-fundal potential

Definition

The electrooculogram (EOG) is an electrophysiological test to assess the standing potential of the eye that normally exists between the cornea and Bruch's membrane at the back of the eye. This potential, also called corneo-fundal potential, is largely derived from the activity of the retinal pigment epithelium (RPE) and depends upon the functional and morphological integrity of the RPE as well as on the interactions between the RPE and the photoreceptors. Since the standing potential of the eye cannot be measured directly in humans, the clinical EOG is used to measure the effects of the state of adaptation upon the standing potential. The EOG voltage is measured first in darkness and then during adaptation to bright background. The ratio between the maximal EOG voltage under light-adapted conditions and the minimal value measured in darkness is called the Arden ratio and was shown to be a reliable measure of the integrity of the RPE and the interactions between the RPE and the photoreceptors.

Purpose

The purpose of recording the electrooculogram in clinical electrodiagnosis of vision is to assess the integrity of the RPE and the interaction between the RPE and photoreceptors. This is achieved by measuring the dependence of the EOG upon the state of adaptation. Therefore, the EOG belongs to the ensemble of electrophysiological tests (ERG, EOG, and Visual Evoked Potentials (VEP)) that are used in electrodiagnosis of visual disorders for assessing retinal function in health and in disease.

Since the electooculogram is a useful tool to track eye movements, it is used for additional purposes including:

1. Following reading strategies in children suffering from learning disabilities.
2. Studying strategies for scanning pictures.
3. Tracking eye movements during sleep to assess sleep disorders.
4. Monitoring fixation quality in experiments involving visual task performance.

Principle

The eye is an electrical dipole in which the cornea is constantly positive compared to the back of the eye. The corneo-fundal potential originates from the metabolic activity of several epithelial tissues within the eye, including the cornea, lens, and RPE, but the RPE component, called the Trans Epithelial Potential (TEP), is the dominant one and is the only one that changes with the state of adaptation. Typically, the standing potential of the eye substantially decreases during dark adaptation, reaching its lowest potential after 8–12 min, a minimum called "dark trough." When a bright background light of about 100 cd/m^2 for dilated eyes and 400 cd/m^2 for non-dilated eyes is turned on, the resting potential gradually rises, reaching a peak in about 9–12 min followed by a slow decline toward baseline level. The standing potential in the dark reflects differential permeability to ions of the apical and basal membranes of the RPE, mainly to potassium ions, and the activity of ionic transporters. The slow rise of the standing potential under background conditions reflects depolarization of the basal membrane of the RPE which is believed to reflect increase in permeability to chloride channels in the basal RPE membrane. Conflicting results from animal models argue about the role of the bestrophin protein in the rise of the standing potential during background light.

The EOG is measured clinically by a pair of electrodes attached to the skin on the left and right sides of the eyes. The patient is instructed to shift gaze, without moving the head, between two red LEDs lighted sequentially to the left and right of the center of fixation. The two target LEDs are separated by about 30°, 15° on each side of the central fixation. With the cornea being positive compared to the back of the eye, horizontal eye movements shift the electrical potential measured between these electrodes in a square wave pattern. In a typical electrodiagnostic setup, the patient first performs the EOG under background conditions for 2–3 min, followed by complete darkness for about 15 min. Then, the background light is turned on and the patient continues with the test for an additional 15 min. Eye movements between the LED targets are typically repeated for 10–15 s every minute.

The amplitude of the voltage changes during eye movements depends upon the resistance of the electrodes, their distance from the eye, and the performance of the task by the patient. To overcome technical variability, Geoffrey Arden suggested in 1962 to measure the "dark trough" and the "light peak" in order to calculate the "light peak" to the "dark trough" ratio, thereby circumventing any technical factors. In visually normal subjects, the value of Arden ratio should be 2.0 (200%) or higher. An Arden ratio lower than 1.8 (180%) is considered abnormal for individuals under the age of 60 years, and a ratio of less than 1.7 (170%) is abnormal for individuals over 60 years of age.

A normal EOG test is shown in the figure. The volunteer performed eye movement for 15 s in about every minute, and the voltage difference of the square wave was plotted as data points in the upper panel. The dark fall toward the "dark trough" in the EOG amplitude during the 15-min dark period followed by the light rise during 15 min of bright background toward the "light peak" are clearly evident. Two examples of the square wave produced by the eye movements between the two red LEDs are shown in the figure; one was recorded during the "dark trough" and the other during the "light peak." In this particular example, the Arden ratio (light peak divided by dark rough) was 4.53 (453%).

Over the years, several attempts were made to use pharmacological approach to affect the transepithelial potential of the RPE directly. Intravenous infusion of hyperosmotic solution and acetazolamide or bicarbonate solution induced a decrease in the EOG voltage. By combining measurements of the EOG light rise with a pharmacologically induced change in the EOG, a better localization of the underlying pathological process can be achieved. Thus, in cases of retinitis pigmentosa, the EOG light rise is absent while acetazolamide-induced decrease in EOG amplitude persists indicating that the source of the abnormal EOG resides in the photoreceptors and not in the RPE.

Indication

The electooculogram is a useful adjunct to electroretinography (ERG) and is typically used for specific indications. It reflects a pan-retinal response and is generally affected in diffuse disorders of the RPE and the photoreceptors. It may be abnormal in conditions characterized by rod dysfunction, chorioretinal atrophy, and inflammation. However, in most of these cases, an abnormal EOG is associated with an abnormal ERG, and there is no need for EOG testing to make a diagnosis.

The hallmark of dissociation between EOG and ERG is Best vitelliform macular dystrophy, which is the most common indication for EOG testing. In Best disease, the "light peak" of the EOG is reduced, giving rise to an Arden ration considerably lower than 1.8 (180%), whereas the ERG is normal because the peripheral retina functions normally. Other diseases associated with abnormal EOG in the presence of normal ERG include autosomal recessive bestrophinopathy, fundus flavimaculatus, and pattern dystrophy of the RPE. The EOG may also be markedly depressed in acute zonal occult outer retinopathy (AZOOR).

Another important use of the EOG is in separating retinitis pigmentosa (RP) and allied disorders from congenital stationary night blindness. It may also be helpful in RP cases that are characterized by a very slow progress of photoreceptor degeneration, and the fundus appearance is atypical for the disease. With patients complaining of difficulties at night and the ERG responses not dramatically reduced in amplitude, a progressive photoreceptor degeneration disorder can be misdiagnosed as stationary night blindness. The EOG is a decisive test since the Arden ratio is subnormal in RP and normal in stationary night blindness.

Contraindication

There is no contraindication for the use of EOG in terms of patient safety. However, for a patient suffering from severe photophobia, the light phase of the test may be too difficult to bear, and the EOG test is useless. Additionally, patients with difficulties in eye movements cannot comply with the EOG procedure and should not be subjected to the test.

Advantage/Disadvantage

The test is noninvasive and provides valuable information in certain cases of retinal disorders.

The validity of EOG results depends on accurate and consistent tracking of the fixation lights, while moving the eyes only and avoiding any head movements for over at least 30 min, and thus this test is not appropriate for young children and for elderly patients. The test also depends on a minimum degree of light adaptation and may not be reliable in patients with severe photophobia who cannot open their eyes during the background phase of the test.

Cross-References

- ▶ Best Vitelliform Macular Dystrophy
- ▶ Electroretinogram
- ▶ Retinal Pigment Epithelium
- ▶ Retinitis

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Electroretinogram

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Synonyms

The electrical response of the retina to a light stimulus

Definition

The visual system processes visual information as patterns of electrical activity. The photoreceptors of the retina transform the physical stimulus (light) into electrical signals that are preprocessed by the retinal neurons before being transferred via the optic nerve to the visual cortex of the brain for further processing. The electrical activity generated in the different types of retinal neurons in response to a light stimulus gives rise to radial extracellular currents that can be recorded by a corneal electrode. This electrical signal is called the electroretinogram (ERG).

The full-field ERG (ff-ERG) response, which is mostly used for electrodiagnosis of retinal disorders, is a summated wave of three major components. The cornea-positive P-I arises from potential change across the retinal pigment epithelium (RPE) reflecting changes in the electrolyte composition of the extracellular space of the retina. The cornea-positive P-II component is generated by electrical activity in post-photoreceptor cells, mainly in the ON-center bipolar cells, and the cornea-negative P-III component reflecting light-induced electrical activity in the photoreceptors. There are additional contributions to the ERG, but these are minor and recorded only under special conditions. The summation of the three ERG components results in the general ERG pattern seen in response to a light stimulus, consisting of an initial negative a-wave, followed by a positive b-wave, and ending with a slow positive c-wave. However, under normal clinical testing conditions, the c-wave is practically absent, and therefore the ff-ERG trace is composed of a negative a-wave followed by a positive b-wave. With bright light stimulus, fast oscillations of small amplitude can be identified on the rising phase of the b-wave. It is customary to use the amplitude and implicit time (latency) of the a-wave for assessment of photoreceptor function and the amplitude and implicit time (latency) of the b-wave as indicators for ON-center bipolar cells' function and for signal transmission between the photoreceptors and the bipolar cells. The fast oscillatory potentials are generated by neural networks in the inner retina between bipolar cells, amacrine cells, and ganglion cells and are very sensitive to the integrity of retinal blood circulation.

Purpose

The ERG is used as an objective method to reliably monitor retinal function in order to identify retinal disorders, to assess severity of retinal diseases, to monitor disease progression, and to track retinal function during treatment. By controlling the color and intensity of light stimulation, the conditions of illumination and pattern of stimulation, the ERG can be used to separate between the function of the rod system from that of the cone system and to isolate the contribution of the peripheral retina from that of the macular region. Furthermore, the ERG can serve to identify the retinal structures that are affected by the pathological process, e.g., photoreceptors, bipolar cells, inner retinal neurons, and ganglion cells. Thus, ERG measurement is an important procedure within the ensemble of electrophysiological tests (ERG, EOG, Visual Evoked Potentials (VEP)) that are used in centers for electrodiagnosis of visual disorders.

Principle

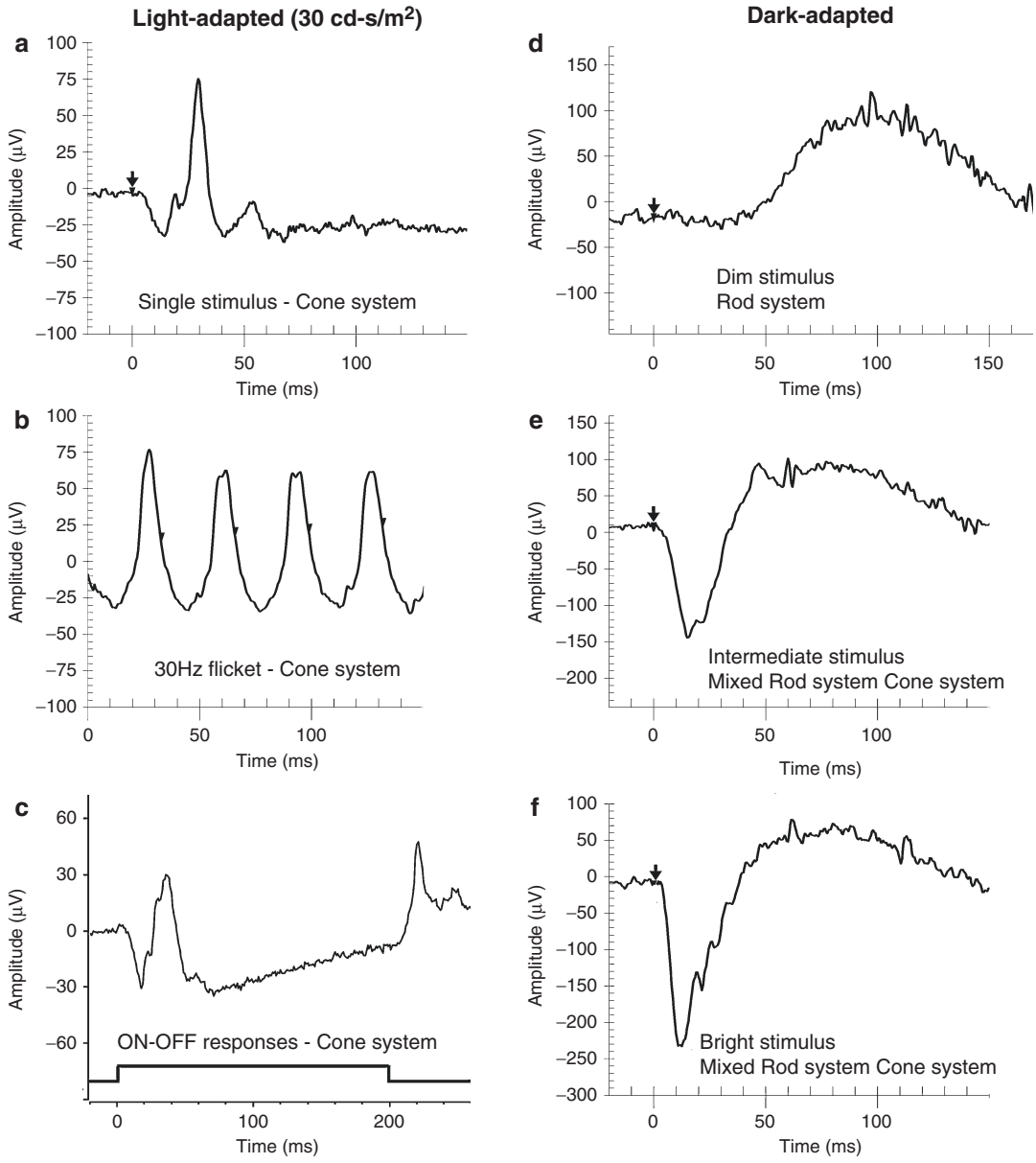
The visual pigment molecules located in the outer segments of the photoreceptors absorb impinging light and, through a cascade of reactions termed the phototransduction process, generate an electrical signal that is transmitted via chemical and electrical synapses to horizontal cells and bipolar cells, which in turn transmit electrical signals to amacrine cells and ganglion cells in the inner retinal layers. The axons of ganglion cells form the optic nerve that carries visual information coded by action potentials to the visual cortex of the brain for further processing. Light-induced electrical activities of retinal neurons generate extracellular radial currents that summate and flow from the retina through the vitreous to the cornea and return to the back of the eye to form the basis for the corneal electroretinogram. Therefore, any resistance to electrical current flow in this pathway, such as silicone oil fill in the vitreous cavity, will be expressed in reduction of the ERG signal down to non-measurable levels even if the retina functions normally.

The most common procedure to record the ERG in clinical settings involves the use of three electrodes, an active corneal electrode, a reference electrode, and a ground electrode. The recorded signal is amplified and filtered by an appropriate data acquisition system. To obtain maximal ERG signals and enable reliable comparison between subjects, full pupillary mydriasis is needed.

The choice of corneal electrodes varies between visual electrodiagnostic centers and depends upon the clinical consideration and patient cooperation. The Burian-Allen bipolar contact lens electrode is the one giving the largest response and the least noisy one, but it is not disposable and requires cleaning and disinfection between recording sessions. Commonly used disposable electrodes include the Dawson, Trick, and Litzkow (DTL) electrode, the gold foil electrode, ERG jet electrode, and others. Some centers use skin electrodes, especially for children and infants in which the active electrode is placed on the skin below the eye. In this case, the recorded signal is typically of small amplitude and high level of electrical noise, and therefore averaging of many repetitions is required for reliable assessment of retinal function.

The waveform of the ERG depends upon the pattern (color, intensity, and duration) of the photic stimulation and upon the conditions of visual adaptation. A dome producing a full-field homogenous stimulus is used to elicit full-field ERG responses that reflect the summed activity of the entire retina and can be used to separate the activity of the rod system from that of the cone system and the cone ON pathway from the cone OFF pathway as shown in Fig. 1. The most useful procedure for ff-ERG recording is described in the ff-ERG standard that is supported by the International Society for Clinical Electrophysiology of Vision (ISCEV), but many visual electrodiagnostic centers adopt a modified version of this standard.

A white background of 30 cd/m^2 saturates the rod system, thus isolating the responses of the cone system (Fig. 1 left column). For reliable assessment of the cone system's function, light adaptation of 10 min is needed. The retinal electrical response to a single flash or to a 30 Hz flicker of stimuli (Fig. 1a, b respectively) serves as good indicators for the functional integrity of the cone system. After at least 20 min of dark adaption, the rod system recovers to about 90% level, and the dark-adapted ERG responses can be recorded (Fig. 1, right column). Under these conditions, the retinal response to a dim white or blue light stimulus is used to assess the function of the rod system (Fig. 1d), while bright white light stimuli elicit ERG responses, which reflect the combined contributions of the rod system and the cone system (Fig. 1e, f), with predominant contribution by the rod system. In some visual electrodiagnostic centers, stimuli of very high intensity (energy) are sometimes used to elicit ERG responses when retinal function assessment is needed in cases of opaque optic media. Additionally, very bright stimuli are used in order to elicit ERG response of saturated a-wave that can be used to derive information about the responsiveness to light of rods or cones.



Electroretinogram, Fig. 1 Full field (ff)-ERG responses from a subject with normal vision. Light-adapted ff-ERG responses are recorded under background illumination of 30 cd/m^2 using single flash of 3 cd-s/m^2 strength (**A**) or 30Hz flicker of 3 cd-s/m^2 strength (**B**). A long-duration (200 msec) stimulus of 200 cd/m^2 (**C**) is used to separate the response of the cone ON-pathway from the cone OFF-pathway. Rod function is assessed from dim blue flash delivered after at least 20 minutes of adaptation to darkness (**D**). Mixed Rod-Cone function is represented by the responses to flashes of intermediate (3 cd-s/m^2) and bright (30 cd-s/m^2) strengths (**E** and **F** respectively)

The full-field ERG recording procedure can be further modified in cases when the ON and OFF pathways of the cone system need to be separated, such as in complete and incomplete congenital stationary night blindness and in melanoma-associated retinopathy (MAR). In these cases, a long duration (200 ms) stimulus is used under light-adapted conditions (Fig. 1c), to generate a

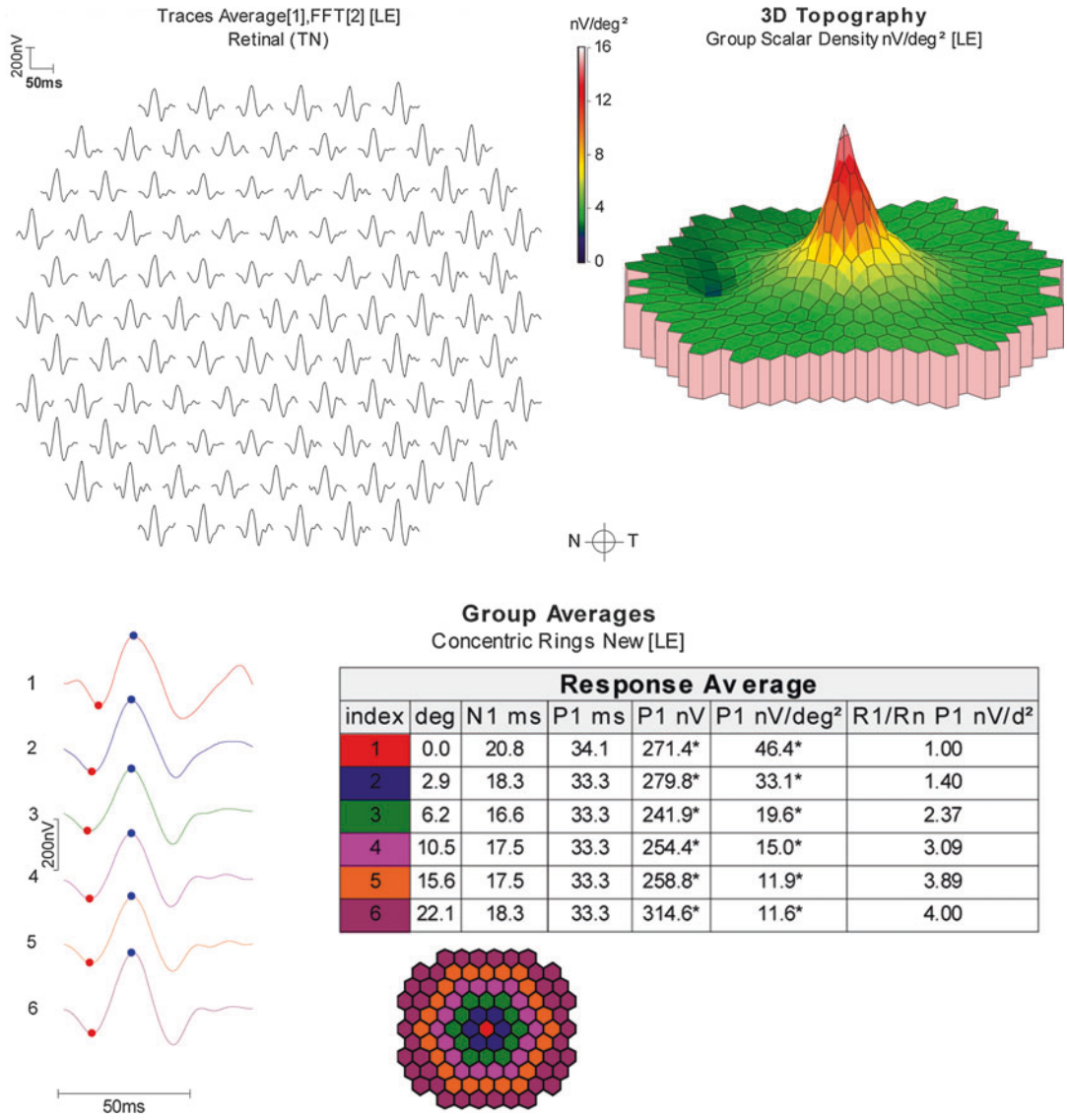
two-component response. The initial response to light onset is composed of an a-wave followed by a b-wave reflecting light-induced activity in the cones and the cones' ON-center bipolar cells. This is the ON-pathway response. At light offset, another positive wave is recorded, called the d-wave, reflecting the activation of cones' OFF-center bipolar cells and the termination of electrical activity in the cones. This is the OFF-pathway response.

Changing test parameters such as the duration, color, and intensity of the light stimulus and/or of the background, the duration of dark adaptation and pattern of the stimulus are used for recording of specific responses to assess function of specific retinal structures, e.g., ganglion cells in the macula (pattern-reversal ERG), ganglion cells in the entire retina (photopic negative response, PhNR), absolute rod sensitivity (scotopic threshold response, STR), and isolated function of the S-cones' system.

Since the ff-ERG is a global response reflecting the summated activity of the entire retina; it is noteworthy that focal retinal lesions will not be identified by a reduced ERG response unless at least 20% of the retina is damaged. Therefore, the ff-ERG is used in suspected pan-retinal disorders, such as photoreceptor degeneration, night blindness, melanoma- or cancer-associated retinopathy, and more. In order to obtain ERG responses that are more sensitive to local retinal damage, the multifocal ERG (mf-ERG) procedure was developed. In this procedure, the light stimulus viewed by the patient comprises an array of hexagons (typically 103 or 61) flickering individually between dark and light at a pseudorandom sequence. The size of the hexagons increases gradually with increasing distance from the center of the array to inversely fit the gradient of the retinal cone density decreasing from the foveal center. In this manner, the focal response of each hexagon is expected to be of similar amplitude in volunteers with normal vision. During stimulation, a single corneal electrode continuously records the electrical potential at the cornea in response to the flickering array of hexagons. Upon termination of the test, the electrophysiological system derives the local ERG responses by comparing mathematically the response at a given time frame to the hexagons' illumination pattern at that time frame relative to that at a previous time frame. With this analysis, an electroretinographical map of the stimulated retinal region is derived as shown in Fig. 2. During the recording procedure, the average screen illumination is stable, similar to the room light, and therefore the ERG responses reflect local function of the cone system. Figure 2 shows mf-ERG data from a volunteer with normal vision, using 103 hexagons flickering between 400 and 0 cd/m^2, covering the central 48° of the retina, roughly parallel to the 24-2 visual field test. The individual responses of the 103 hexagons (Fig. 2, upper left) represent the average ERG response at each hexagon. These responses are recalculated as amplitude density (response amplitude divided by hexagon area) in order to derive the colored 3D surface map (Fig. 2, upper right) indicating high activity of cone system in the center (fovea) that tapers off to a steady low value at eccentricities ranging from 5 to 24° reflecting the normal retinal distribution of the cone system in the human retina. With the assumption that the cone system reduces similarly along radial paths originating at the fovea and extending to large eccentricities, it is customary to sum the activity at concentric rings and calculate it as amplitude density by dividing the ring amplitude by the ring area (Fig. 2 bottom left). The attached table indicates the eccentricity of each ring, implicit times of N1 and P1 waves, average amplitude for each ring, amplitude density for each ring, and ring ratios. Excellent patient cooperation and stable fixation are necessary for reliable results of the mf-ERG procedure. Good fixation is verified by localization of a small depression in the 3D map (Fig. 2 upper right panel), about 15–20° nasal to the fovea, representing the blind spot at the optic disk. The mf-ERG is sensitive to local retinal damage and is used to test maculopathies and cases presenting with local scotomas in the central visual field (24-2).

Indication

Any patient that complains of visual disturbances that cannot be explained by routine tests available



Electroretinogram, Fig. 2 Multifocal ERG measurement from a subject with normal vision. The central 48° of the retina are illuminated by 103 hexagons, and the retinal response is analyzed and presented as the trace array (*upper left*). The 3D plot of the retinal response generated by each hexagon (*upper right*) clearly shows the peak amplitude density of the fovea, and the slight depression in the nasal retina representing the optic disk. The trace array is divided into 6 rings centered on the fovea (central hexagon). The rings' ERG responses, shown in the lower left side, represent the average response to each hexagon in the ring. The Table lists for each ring, the average eccentricity from the fovea, implicit time of N1 and P1, P1 average amplitude, P1 amplitude density and ring ratio relative to Ring1, the central one

in the ophthalmic clinic may potentially benefit from ERG testing.

The most common indications for ERG testing are:

1. Visual difficulties at night – assess scotopic function using ff-ERG.
2. Photophobia in daytime – assess photopic function using ff-ERG.

3. Unexplained loss of visual field – test first with ff-ERG, and if normal, try mf-ERG.
4. Symptoms of flashes, shimmering lights – use ff-ERG to test for cancer-associated retinopathy (CAR), melanoma-associated retinopathy (MAR), or other types of autoimmune retinopathy (AIR).
5. Test for chloroquine (Plaquenil) toxicity using mf-ERG.
6. Unexplained reduction in visual acuity or subjective complaints of decreased central vision – use mf-ERG to test for maculopathy.
7. Asymptomatic relatives of patients with known inherited photoreceptor degeneration – use ff-ERG to test for the disorder.
8. Separate fundus albipunctata from fundus punctata albescens using ff-ERG.
9. Evaluation of retinal function prior to a complex eye surgery – use ff-ERG; sometimes bright flash ERG is needed.

Contraindication

There are no contraindications for the use of ERG and no known patient safety concerns. However, there are several contraindications for specific procedures. A patient suffering from epilepsy should not be tested with 30 Hz flicker at light-adapted ff-ERG procedure or with mf-ERG. Patients with corneal wounds and patients after corneal surgery including photorefractive surgery (especially Laser In Situ Keratomileusis (LASIK)) should not be tested with the corneal contact lens electrode. Patients with severe eye infection should be tested with a disposable electrode.

Advantage/Disadvantage

Advantages

1. Objective test of retinal function
2. Can be used to monitor reliably over time disease progression, efficacy of treatment, and drug toxicity
3. Can separate photopic function from scotopic function
4. Can separate function of peripheral retina from that of macular region
5. Allow assessment of function in specific retinal structures, e.g., photoreceptors, bipolar cells, inner retinal neurons, and ganglion cells

Disadvantages

1. Intersubject variability
2. Intra-subject variability between consecutive recording sessions

E

Cross-References

- ▶ Bipolar Cells
- ▶ Bright-Flash Electroretinogram
- ▶ Cancer-Associated Retinopathy
- ▶ Chloroquine Toxicity, Cornea Verticillata
- ▶ Congenital Color Vision Defects
- ▶ Dark Adaptation Testing
- ▶ Fundus Albipunctatus
- ▶ Light Adaptation
- ▶ Macular Dystrophy
- ▶ Nyctalopia: Night Blindness
- ▶ Retinal Peripheral Degeneration
- ▶ Retinal Pigment Epithelium
- ▶ Retinitis
- ▶ Retinitis Punctata Albescens
- ▶ Usher Syndrome

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Elschnig Spots

Sign of Acute and Chronic Hypertensive Choroidopathy

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Synonyms

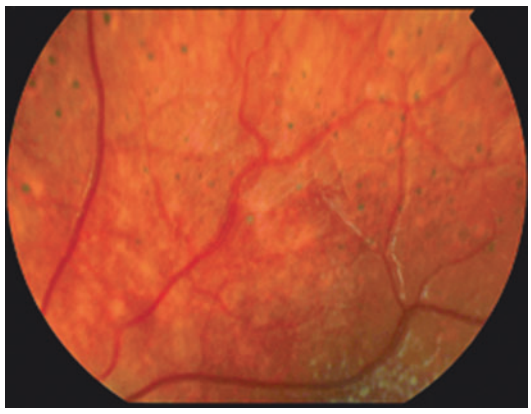
Ischemic infarct of the choroid

Definition

Elschnig spots are changes in the retinal pigment epithelium from non-perfused areas of the choriocapillaris in hypertensive choroidopathy. Their appearance is pale or yellow and tends to have defined margins. When an Elschnig spot heals, a scar develops, and a pigment spot is left surrounded by a depigmented pale halo (Fig. 1).

Etiology

Acute and chronic hypertension may manifest in the eye as hypertensive retinopathy and choroidopathy. The effects of hypertension on the choroid are related to the anatomic and functional differences found in the choroidal vasculature, as compared with the retinal vasculature. Sympathetic innervation of the choroid makes terminal arterioles more susceptible to vasoconstriction, and the lack of autoregulation increases susceptibility to elevated perfusion pressures. Circulating vasoconstrictive factors such as angiotensin II, adrenaline, and vasopressin can initiate vasoconstriction of the choroid and choriocapillaris, leading to focal ischemia. Fenestrations in the choroidal capillaries and the consequent lack of a blood-ocular barrier allow free passage of macromolecules. As a result the overlying retinal pigment epithelium (RPE) and the outer blood-retinal barrier may be compromised. In the acute phase, this can lead to a local leakage of fluid from the choroid into the subretinal space forming serous detachments (Bourke et al. 2004; DellaCroce and Vitale 2008; Ugarte et al. 2008).



Elschnig Spots, Fig. 1 Elschnig spots in the mid-periphery, seen at 4 months after presentation of malignant hypertension in a child (Courtesy of D.A. Morisson et al.)

Elschnig spots develop from damage to the retinal pigment epithelium overlying a local area of ischemia in the choriocapillaris caused by choroidal infarcts (Shah et al. 2011). Elschnig spots are commonly observed in the posterior pole. These changes are different from the more superficial retinal infarcts ("cotton wool spots") and retinal hard exudates observed in accelerated and chronic hypertension. Over time an Elschnig spot heals leaving a pigment spot surrounded by a depigmented pale halo (Bourke et al. 2004; DellaCroce and Vitale 2008; Ugarte et al. 2008; Shah et al. 2011).

Fluorescein angiography (FA) is used to confirm ophthalmoscopic suspicion of hypertensive choroidopathy. Early in their development, Elschnig spots display hyperfluorescence on FA because of leakage from focal compromise to the blood-retina barrier. After the initial damage heals, the hyperfluorescent FA pattern changes to be more consistent with a window defect from overlying RPE atrophy (Bourke et al. 2004; Ugarte et al. 2008).

Hypertension control and management needs to be the first goal of treatment, but carotid ischemia and temporal arteritis should also be considered.

Occurrence

Hypertensive choroidopathy and Elschnig spots occur later than the retinal vascular changes (hypertensive retinopathy) of arteriolar narrowing and arteriovenous crossing changes in chronic hypertension. These advanced abnormalities are observed more commonly in younger patients with acute increases in blood pressure and are associated with a poor prognosis in the untreated hypertensive patient. Hypertensive choroidopathy has been reported in association with toxemia of pregnancy, chronic glomerulonephritis, pheochromocytoma, and malignant hypertension (Bourke et al. 2004; DellaCroce and Vitale 2008; Ugarte et al. 2008; Shah et al. 2011).

Classification

Clinical feature of hypertensive choroidopathy

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Emmetropia: Definition

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Definition

Emmetropia is the term used to describe the condition of absence of refractive errors. That means that an object point located at infinity is sharply imaged to the retinal plane in absence of accommodation. Refractive correction (e.g., spectacle correction, contact lenses) is not required. In practice emmetropia is defined for a range of ±0.25 diopters or refraction.

Cross-References

▶ Ametropia: Definition
▶ Diopter: Definition
▶ Refractive Errors

Emphysema (Ocular), of Orbit and Eyelids, in Blowout Fractures

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Synonyms

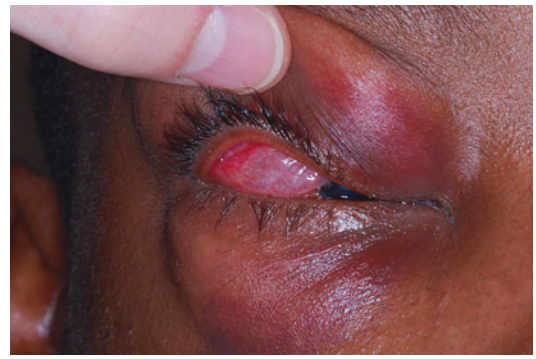
Pneumo-orbitism

Definition

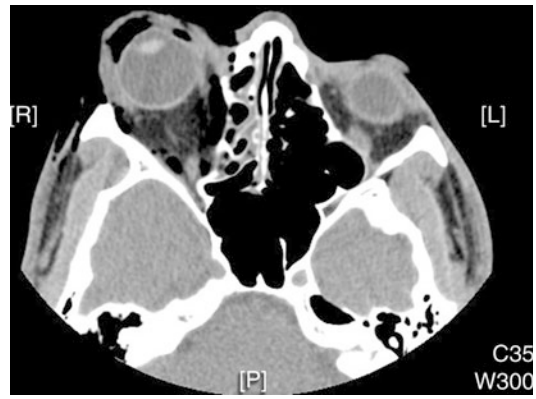
Presence of air in the orbit and/or periorbital tissues following orbital wall fracture.

Etiology

Orbital blowout fractures occur when an impact raises intraorbital pressure to the point where the thin bones of the orbital floor and medial wall are "blown out," pushing orbital contents into the maxillary or ethmoid sinus (Nerad et al. 2001). Orbital emphysema most commonly results from an orbital blowout fracture (63% of cases; Key et al. 2008). The resulting communication with the paranasal sinuses allows air to accumulate in the orbital space. Sudden onset of orbital emphysema after Valsalva maneuvers (laughing, sneezing, nose blowing) is occasionally reported and is believed to result from the formation of a one-way valve across the fracture site, permitting air to enter the orbit, but not to leave it. Orbital emphysema has also been reported after sinus surgery.



Emphysema (Ocular), of Orbit and Eyelids, in Blowout Fractures, Fig. 1 Orbital emphysema with air pockets noted in the subconjunctival space of the superior forniceal space



Emphysema (Ocular), of Orbit and Eyelids, in Blowout Fractures, Fig. 2 CT scan of patient in Fig. 1, demonstrating intraorbital (preseptal and postseptal) emphysema

Clinical Presentation

Classically, patients who have had recent trauma to the orbit, face, or head present with sudden onset of one or more of the following after nose blowing, laughing, or other Valsalva actions: periorbital swelling, pain, lid distension, diplopia, and blurred vision. On examination, patients may demonstrate decreased visual acuity; ophthalmoplegia; a tense, hard globe; and proptosis. Emphysema may be palpable within the eyelids as crepitus and may be visible in the subconjunctival space (Fig. 1). Intraocular pressure (IOP) is usually elevated. If high intraorbital air pressure results in decreased perfusion to the retina or optic nerve, an afferent pupillary defect may be present (Muhammad and Simpson 1996).

Orbital emphysema may also present as an incidental finding on radiographic assessment; it is detected in up to 50% of orbital fractures on CT scan (Fig. 2; Key et al. 2008).

Diagnostics

The diagnosis of orbital emphysema can usually be made from history and physical examination alone. However, distinguishing orbital emphysema from retrobulbar hemorrhage can be difficult; therefore, the diagnosis should be supported by orbital CT scan. IOP should be measured by tonometry, and an assessment of extraocular muscle function should be made.

Differential Diagnosis

Differential diagnosis includes:

Retrobulbar hemorrhage
Orbital cellulitis

Preseptal cellulitis
Thyroid orbitopathy
Benign or malignant orbital tumor
Orbital inflammatory syndrome

Prophylaxis

Patients with recent orbital and facial trauma, with or without radiographic evidence of orbital wall fracture, should be advised to avoid nose blowing, heavy lifting, laughing, and other Valsalva activities.

Therapy

Orbital emphysema without visual loss is a benign, self-limited condition, which usually resolves in about 2 weeks. Mildly elevated IOP with no associated visual deficits can be observed or treated medically with IOP-reducing topical agents. However, compressive orbital emphysema with rapidly decreasing visual acuity is an emergency and must be treated promptly to avoid ischemic damage to the retina and optic nerve. Surgical decompression is achieved via lateral canthotomy and cantholysis, which expands the orbital volume and lowers intraorbital pressure. In rare cases, intraorbital needle aspiration may be necessary to relieve compression (Key et al. 2008).

Antibiotics may reduce the incidence of orbital cellulitis in cases of orbital emphysema; however, the benefit of antibiotics remains unproven (Key et al. 2008).

Prognosis

Orbital emphysema is generally a benign, self-limiting condition with an excellent visual prognosis (Muhammad and Simpson 1996). Nearly all reported cases of orbital emphysema with subsequent optic nerve compression showed complete recovery of visual acuity.

Epidemiology

Orbital emphysema is most commonly seen after orbital floor and/or medial wall fractures. It is detected in up to 50% of orbital wall fractures on CT scan (Key et al. 2008). Very few cases of orbital emphysema with optic nerve compression have been reported.

Cross-References

- ▶ Orbital Floor Fracture
- ▶ Proptosis
- ▶ Retrobulbar Hemorrhage

References

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Encircling Buckle

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Synonyms

Scleral buckle

Definition

Scleral buckling is an ophthalmic surgical technique that has been successfully employed to repair rhegmatogenous retinal detachments for over 50 years. The scleral buckle alters the shape

of the eye, depending on the type of material and explant used to achieve scleral indentation to approximate the detached retina and to achieve functional closure of all retinal breaks, to allow normal physiological processes and to maintain an attached retina.

Encircling buckle is defined as a 360° encircling, circumferential silicon band passed around the circumference of the globe and beneath the rectus muscles.

Indication

An encircling buckle is used in cases of rhegmatogenous retinal detachment with single or multiple defects and also in patients with early proliferative vitreoretinopathy and very extensive scleromalacia. Extensive retinal detachment which breaks is difficult to detect. Another indication for using encircling buckle is retinal detachment due to dialysis.

Contraindication

Retinal breaks significantly posterior to the equator are difficult to approach due to anatomic location. Patients with significant vitreoretinal proliferation and vitreous traction are difficult to treat only with scleral buckle reducing the rates of success; these patients can be approached by a combination of scleral buckle with vitrectomy. Opaque media obscures a good visualization of the retinal tears and good placement of the scleral buckle.

Techniques and Principles

1. A circumferential 360° peritomy with radial relieving incisions is made.
2. Slinging of rectus muscles employing a special muscle hook, a large bridle suture (2–0 silk) is passed under the rectus muscle to stabilize the globe.
3. Careful indented examination under anesthesia of the whole peripheral retina is now carried out to determine the location of the retinal breaks; every break is marked on the sclera.
4. Retinopexy is required to produce an enduring bond between the retina and the retinal pigment epithelium. Cryotherapy is used to create this, under direct visualization of indirect ophthalmoscope; after localizing the retinal break, we indent the sclera with the cryoprobe, and after revalidation of position over the break, the cryoprobe is activated. After a few seconds, one observes whitening of the retina. If the tear is small, one application can be enough; most of the times several cryotherapy applications should be made to ensure complete retinopexy.
5. Next, the tire and band are threaded together under the recti and mattress sutures. Ensure that both limbs of all the mattress sutures are above the buckle as it is not uncommon to leave one under the encirclement by mistake.
6. Scleral sutures are placed in each quadrant to accommodate the encircling silicone tire and its silicon band. The anterior suture bite is placed at the estimated location of the ora serrata, and the posterior bite is placed far posteriorly, at a spot dictated by the width of the tire, the desired amount of indentation, and the location of tears. Frequently, this distance is equal to twice the distance from the anterior bite to the marked posterior edge of the retinal break. Calipers are used to ensure accurate bite separation. The sutures need to be placed halfway through the sclera to prevent perforation.
7. Subretinal fluid drainage is required in the majority of cases.
8. Tighten the mattress sutures over the tire to create a local indent.
9. The ends of an encircling band are joined with a silicone Watzke silicone sleeve, tantalum clip, or suture; a Watzke sleeve is a small Silastic tube designed to secure the ends and allow adjustment of the tension in the band.
10. The ends of the band are pulled to create the encircling indent. A 6-mm shortening will produce approximately a 1-mm indent, irrespective of the size of the globe.

Final examination of the retina needs to be done to evaluate height of the buckle, correct positioning over the break, and perfusion of central retinal artery.

Trimming of any protruding edges needs to be done to reduce the risk of buckle extrusion; also good closure of Tenon's capsule and conjunctiva needs to be achieved.

Outcome

A favorable anatomic reattachment is achieved in 90% of cases; although, there is a significant discrepancy between favorable anatomic correction and functional visual outcomes, this can be correlated with macular involvement.

Complications

Two different groups of complications can be present, intraoperative and postoperative complications.

Intraoperative complications such as scleral perforations in the process of anchor scleral sutures and penetration of the globe are usually heralded by the sudden appearance of subretinal fluid at either end of the suture bite; it can lead to choroidal hemorrhage.

If the surgeon decides to do a drainage procedure, it should be performed with subtle care to prevent hemorrhage, retinal incarceration, and iatrogenic retinal holes. In the setting of a high encircling buckle and a horseshoe tear, "fishmouthing" of retinal breaks can be present, in which the open break will prevent a complete retinal reattachment.

In postoperative complications, the most important one is anatomic failure, followed by increased intraocular pressure, choroidal detachment, and late periocular infection and implant extrusion, because the various materials used in scleral buckle technique (sutures, bands) are foreign bodies.

Another common complication is formation of epiretinal membranes; macular pucker has been reported from 2% to 17% of successfully treated retinal detachments. Failure of the retina to reattach or recurrent retinal detachment can be due to proliferative vitreoretinopathy.

Due to the configuration of circumferential scleral buckle, an altered refractive error can occur, usually causing a myopic change due to changes in axial length; every 1 mm of average increase in axial length can cause a −2.50 diopters of myopic shift.

Cross-References

▶ Retinal Detachment
▶ Scleral Buckle

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Endoepithelial Corneal Dystrophy

▶ Fuchs' Dystrophy Disease

Endogenous Endophthalmitis

▶ *Aspergillus* (Aspergillosis), Endogenous Endophthalmitis
▶ *Candida* (Candidiasis), Ocular Infection/Inflammation Caused by, Endogenous Endophthalmitis

Endogenous Infectious Endophthalmitis

▶ Bacteria, Endophthalmitis Caused by, Endogenous

Endophthalmitis

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Synonyms

Intraocular infection

Definition

Infectious inflammation of the ocular cavities and internal structures of the eyeball.

Histology

Inflammatory infiltrates in the vitreous and the retina mainly consist of polymorphonuclear leucocytes. These infiltrates release proteolytic enzymes that destroy all intraocular structures with exception of basal membranes. The underlying pathogen cannot be identified by histology. For acute postoperative endophthalmitis, common bacteria are coagulase-negative *Staphylococci* spp., *Staphylococcus aureus*, *Streptococci* spp., and gram-negative bacteria, for late-onset postoperative endophthalmitis propionibacteria and fungi, and for endogenic endophthalmitis fungi (esp. *Candida albicans* and *Aspergillus* spp.) and *Bacillus* spp (Anon 2005).

Immunohistochemistry

Immunohistochemistry does not play a role in the diagnostics of endophthalmitis.

Electron Microscopy

Remains of the lens capsule or an explanted IOL can be analyzed using scanning electron microscopy (SEM) or transmission electron microscopy (TEM). Though the use of electronic microscopy allows the collection of data related to the physiopathology of the infection, this method is not usually part of the diagnostic routine analyzing the pathogen (Adán et al. 2008).

Molecular Diagnosis

As with any infection, the cornerstone of management of postsurgical endophthalmitis includes identification of the responsible organism. In addition to gram staining and cultures to investigate the underlying microbial organism, samples of aqueous and vitreous can also be analyzed by using polymerase chain reaction (PCR) testing. This technique can increase the laboratory rate of identifying the pathogen. Samples of both aqueous and vitreous should be collected and stored at minus 20° for PCR at the time of the diagnostic tap (Seal et al. 2008).

Differential Diagnosis

An acute postoperative endophthalmitis is rarely misdiagnosed due to often typical anamnestic data and typical clinical appearance. Differential diagnosis includes ocular or systemic sterile inflammatory or malignant conditions that result in an anterior, intermediate, posterior, or panuveitis. The term masquerade syndrome is used for malignant diseases manifesting as an intraocular inflammation of unknown origin. In persistent or refractory ocular inflammation in middle-aged patients, primary intraocular lymphoma should be considered.

Cross-References

► Intraocular Lymphoma
► Secondary Glaucoma in Uveitis

References

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Endothelial Degeneration

▶ Endothelial Dystrophies
▶ Endothelial Failure

Endothelial Degenerations

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Synonyms

Endothelial dystrophy; Fuchs dystrophy; Posterior corneal dystrophies

Definition

Endothelial degeneration is the degradation of the innermost layer of the cornea, the endothelium (Krachmer and Palay 2006). The cornea is composed of several layers: epithelium, Bowman's layer, stroma, Descemet's membrane, and endothelium. The endothelium is typically one cell layer thick and serves to regulate water in the corneal stroma. Damage to this cell layer may result in reduced fluid flow and corneal swelling. This corneal degeneration, or dystrophy, may have hereditary influence and typically cannot be repaired. Descemet's membrane also may be involved with disease. Types of corneal dystrophy involving the endothelium include Fuchs dystrophy, congenital hereditary endothelial dystrophy, and posterior polymorphous corneal dystrophy.

Cross-References

▶ Congenital Hereditary Endothelial Dystrophy
▶ Corneal Degenerations
▶ Fuchs Dystrophy
▶ Posterior Corneal Dystrophies

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Endothelial Dystrophies

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Synonyms

Corneal dystrophy; Endothelial degeneration

Definition

Endothelial dystrophy is the degeneration of the innermost layer of the cornea, the endothelium (Kanski and Bowling 2011). Endothelial dystrophy is a subset of a larger group of corneal diseases called corneal dystrophy. Corneal dystrophy refers to a group of inherited diseases that typically are bilateral, symmetric, progressive, and unrelated to environmental factors (Krachmer et al. 2011). Three major types of endothelial dystrophy include Fuchs dystrophy, posterior

polymorphous dystrophy, and congenital hereditary endothelial dystrophy (Yanoff and Duker 2014). Fuchs dystrophy is a bilateral accelerated loss of endothelial cells, with damage and progression of the disease leading to vision loss and even corneal blindness. Posterior polymorphous dystrophy is a rare and asymptomatic condition where the endothelium cells display epithelial characteristics. Congenital hereditary endothelial dystrophy develops perinatal with a focal or generalized absence of the endothelium.

Etiology

Endothelial dystrophies have been found to have both sporadic and hereditary autosomal causes (Kanski and Bowling 2011). Majority of Fuchs dystrophy tends to be sporadic, while it may have an autosomal-dominant presentation in some families. Congenital hereditary endothelial dystrophy has two main forms, CHED1 (autosomal dominant, 20p11.2–q11.2) and CHED2 (autosomal recessive, 20p13) (Krachmer et al. 2011). Inheritance for posterior polymorphous dystrophy is usually autosomal dominant (three genes, three forms PPCD1–3).

Clinical Presentation

Patients with endothelial dystrophy may present with mild reduction in visual acuity and blurred vision (Krachmer et al. 2011). These diseases progress slowly and symptoms may not become apparent initially. Fuchs dystrophy may be accompanied by worse vision in the morning and improvement over the day (Kanski and Bowling 2011). Ocular pain may also be a factor in some patients due to increased corneal edema and bullae formation. Congenital hereditary endothelial dystrophy develops in the perinatal period.

Diagnosis

Endothelial dystrophy diagnosis requires a thorough clinical evaluation (Kanski and Bowling 2011). A thorough patient history and slit-lamp examination are required. Given a patient's family history, genetic testing may aid in the diagnosis of a particular dystrophy.

On slit-lamp examination, patients with Fuchs may be found to have increased stromal thickness, tiny dark spots revealed as disruption of the regular endothelial mosaic, and a "beaten bronze" endothelium secondary to melanin deposition (Krachmer et al. 2011). Though not part of the clinical diagnosis, histology of the cornea would reveal bullae and corneal edema. Posterior polymorphous dystrophy may reveal signs of subtle vesicular endothelial lesions, band-like lesions, or diffuse opacities. Congenital hereditary endothelial dystrophy has perinatal onset and presents with bilateral, symmetrical, diffuse corneal edema ranging from a bluish-gray ground glass appearance to total opacification.

Differential Diagnosis

Keratoconus, bullous keratopathy, herpetic stromal keratitis, uveitis, congenital stromal dystrophy, pigment dispersion syndrome, and iridocorneal endothelial dystrophy.

Prophylaxis

No known prevention.

Therapy

General treatment for most endothelial dystrophies involves symptomatic and conservative management early on with topical sodium chloride 5% drops or ointment, reduction of intraocular pressure, or even use of a hair dryer in the morning to accelerate corneal dehydration (Yanoff and Duker 2014). Bandage contact lenses are another means for providing comfort due to bullae irritation (Kanski and Bowling 2011) For Fuchs dystrophy, progression of the disease may necessitate surgical procedures, specifically

penetrating or deep lamellar endothelial keratoplasty. Descemet's stripping endothelial keratoplasty (DSEK) or Descemet's stripping automated endothelial keratoplasty (DSAEK) have grown in popularity and are found to have improved results for mild/moderate Fuchs dystrophy. Descemet's membrane endothelial keratoplasty (DMEK) is also emerging as a new surgical treatment for endothelial disease. For posterior polymorphous dystrophy, most disease remains stable (Krachmer et al. 2011). Some patients may require corneal transplantation.

Therapy for congenital hereditary endothelial dystrophy involves penetrating keratoplasty. This procedure has a strong chance for success if performed early for the child. Surgical delay may result in dense amblyopia.

Prognosis

There is no treatment to reverse the progression of endothelial dystrophy (Yanoff and Duker 2014). For posterior polymorphous dystrophy, the majority of patients have stable disease and may remain asymptomatic (Krachmer et al. 2011). Patients requiring surgical intervention may have recurrence. The prognosis overall for recipients of PKP and DSEK is quite excellent (Kanski and Bowling 2011). However, surgical procedures to replace the endothelium carry a risk of graft rejection. Postoperative follow-up is necessary to prevent and treat rejection.

Epidemiology

Endothelial dystrophies affect women and men equally (Yanoff and Duker 2014). However, Fuchs dystrophy affects women roughly four times more than men. Dystrophies may affect all ages. Fuchs in particular affects 4% of the population over 40 years of age (Krachmer et al. 2011). The incidence, prevalence, and sex distribution of posterior polymorphous dystrophy and congenital hereditary endothelial dystrophy are unknown (Yanoff and Duker 2014).

Cross-References

- ▶ Congenital Hereditary Endothelial Dystrophy
- ▶ Corneal Dystrophy
- ▶ Endothelial Degeneration
- ▶ Endothelial Failure
- ▶ Fuchs Dystrophy

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Endothelial Dystrophy

- ▶ Endothelial Degenerations

Endothelial Failure

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Synonyms

Endothelial degeneration

Definition

Corneal endothelial failure occurs with irreversible and compromised endothelial function resulting in severe corneal edema. The endothelium in a healthy individual regulates active water transport away from the corneal stroma toward the aqueous. Early corneal edema may be marked by symptoms of blurry vision as the cornea begins to accumulate fluid and blisters (bullae) secondary to

impaired endothelial function. No medical treatment can promote endothelial regeneration once it has begun to deteriorate. Worsening cell damage due to trauma or disease, such as Fuchs dystrophy, may result in irreversible endothelial failure. Medical management of irreversible endothelial failure involves endothelial replacement with corneal transplantation.

Cross-References

- ▶ Corneal Degenerations
- ▶ Endothelial Degeneration

Endothelial Graft Rejection

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Synonyms

Corneal graft rejection

Definition

Corneal transplantation is the most common form of tissue transplantation (Levin and Albert 2010). Transplant typically is conducted for corneal dystrophy, bullous keratopathy, infection, or failed grafts. Endothelial rejection is the most common form of graft rejection (Brightbill et al. 2009). Immune rejection of corneal grafts is the leading cause of graft failure (Krachmer et al. 2011).

Etiology

While graft rejection is triggered by major histocompatibility antigens for most forms of solid-tissue/organ transplantation, histocompatibility matching of donor tissue for the recipient is variably conducted in the cornea (Levin and Albert 2010). The normal cornea expresses low levels of histocompatibility antigens, specifically HLA antigens. Current studies are inconclusive regarding the benefit of conducting HLA matching for corneal transplants. Of note, minor histocompatibility antigens have demonstrated a role in triggering graft rejection. The pathophysiology of rejection involves antigen presentation to T cells. T cell activation results in graft destruction.

Several causes and risk factors have been found to be associated with endothelial graft rejection. The two most common risk factors are stromal neovascularization and host bed inflammation (Levin and Albert 2010). Corneal neovascularization is linked to high graft rejection, with elevated levels of blood vessels correlating with endothelial rejection (Levin and Albert 2010). Corneal inflammation, both at time of transplant and even prior, is associated with significantly decreased graft survival. Alternative causes for graft rejection are ocular surface diseases, such as severe dry eye, or injury.

Occurrence

Over 70,000 corneal transplants are conducted each year worldwide (Levin and Albert 2010). The average onset for endothelial rejection is 8 months (Brightbill et al. 2009).Rejection may begin as early as 2 weeks or as late as 20 years after transplant. Of the transplants into uncomplicated graft beds, about 20–40% of grafts experience one episode of immune rejection (Levin and Albert 2010). In this normal-risk transplant, only 10% of patients experience rejection by postoperative 1-year mark.

In high-risk, complicated graft beds, 50–90% of grafts fail even with immune suppression (Levin and Albert 2010). These graft beds are complicated by inflammation and neovascularization.

Classification

There are three types of corneal graft rejection: epithelial, stromal, and endothelial (Levin and

Albert 2010). Endothelial graft rejection is the most common. Endothelial surface precipitates can be observed in groups or a classic linear line (Khodadoust line) (Brightbill et al. 2009). This line begins at the periphery of the graft and continues centrally. Endothelial rejection can then result in increased edema and inflammation.

Presenting symptoms include decreased vision, irritation, and eye redness (Krachmer et al. 2011). Edema and signs of precipitates on the donor endothelium are signs of graft rejection. Corticosteroids are the primary treatment for acute cornea allograft rejection. Endothelial rejection can be treated with topical, periocular, and/or systemic corticosteroids.

Cross-References

- ▶ Corneal Degenerations
- ▶ Endothelial Degeneration
- ▶ Endothelial Dystrophy

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Endothelial Keratitis

- ▶ Stromal Keratitis (Herpetic)

Endothelial Keratoplasty (EK)

- ▶ Lamellar Keratoplasty

Enucleation

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Definition

Enucleation is the surgical removal of the eyeball from the orbit.

Indications

There are several indications for enucleation (Moshfeghi et al. 2000). The most common are as follows:

1. Trauma
2. Intraocular malignancy
3. Blind, painful eye
4. All other causes

Trauma

Trauma is a common indication for enucleation and cause of blindness in the USA (AAO 2008). When caring for a traumatized and possibly ruptured globe, it is common practice for surgeons to make all attempts to repair the globe primarily. Sparing the patient primary enucleation serves many purposes. First it allows any subsequent enucleation to be performed under planned and controlled conditions. Also, it allows time for the patient to realize that the traumatized eye is no longer functional. Then he or she can be adequately informed and proper consent obtained as the patient might be disoriented, medicated, or even unconscious in the immediate posttraumatic period. However, if primary repair of the globe is not possible, as may

be seen following gunshot wounds, primary enucleation may be indicated.

Once a traumatized globe has been repaired but it is determined that it will no longer provide useful vision, the decision must be made as to remove that eye or not. If no useful vision is maintained, some surgeons recommend enucleation of the traumatized eye to protect the fellow eye from sympathetic ophthalmia. This rare form of granulomatous uveitis can cause severe visual loss in the fellow or "sympathizing" eye. If the decision is made to enucleate for prevention of sympathetic ophthalmia, it should be performed within 2 weeks of the trauma. Also, although there is a perceived advantage of enucleation over evisceration for prevention of sympathetic ophthalmia, this has never been proven. In fact, cases of sympathetic ophthalmia have been reported after both procedures.

Intraocular Malignancy

Until the late twentieth century, enucleation was the only generally accepted treatment for intraocular malignancy. Although there are now eye-sparing treatments in use, enucleation remains very common. Choroidal melanoma, the most common primary intraocular malignancy of adults, and retinoblastoma, the most common primary intraocular malignancy of childhood, may require enucleation. Also enucleation should be considered for any other intraocular neoplasm with malignant potential that fails to respond to conventional therapy, has metastatic potential, or has resulted in a blind, painful eye.

Blind, Painful Eye

There are numerous causes of a blind, painful eye. Trauma, neovascular glaucoma, chronic retinal detachment, chronic angle-closure glaucoma, retinopathy of prematurity, uveitis, and tumors can all lead to a blind, painful eye. When conservative measures such as topical medications, cyclodestructive therapy, or retrobulbar injection of alcohol or thorazine have failed to control the pain, removal of the eye is considered. Enucleation and evisceration can both be reasonable options and should be chosen on an individualized basis.

Other Indications

Phthisis bulbi, microphthalmia, and improvement of cosmesis are other common indications for enucleation.

Techniques and Principles

Enucleation is usually carried out under general anesthesia (Stewart 1995). A retrobulbar injection of local anesthetic with epinephrine can be used for intraoperative hemostasis and pain control. After creating a 360° conjunctival peritomy, the extraocular muscles are isolated and transected, and the optic nerve is clamped and severed. An orbital implant of sufficient volume is usually placed within the orbital space to account for volumetric changes. The EOMs are usually secured onto the implant, and it is covered by approximating Tenon's capsule and overlying conjunctiva. A conformer is then placed to retain the anatomy of the fornices. After adequate healing, a custom-made prosthesis (i.e., artificial eye) is placed.

Outcomes

The goal of enucleation is to remove the source of pathology while delivering an acceptable cosmetic outcome. Depending on the indication for enucleation, appropriate pathology specimens are obtained and further treatment, both locally and systemically, may be indicated. An ocular prosthesis is usually fitted by an ocularist 6 weeks postoperatively in order to provide a good cosmetic result.

Complications

Complications can occur intraoperatively and postoperatively. Intraoperative complications include removal of the wrong eye, a slipped extraocular muscle, and orbital hemorrhage. Postoperatively, hemorrhage, edema, and infection can complicate the early course while enophthalmos, superior sulcus deformity, and implant exposure and extrusion can occur months to years after the initial surgery.

Cross-References

- ▶ Angle-Closure Glaucoma
- ▶ Choroidal and/or Ciliary Body and/or Iris Melanoma
- ▶ Evisceration
- ▶ Implants, Orbital
- ▶ Neovascular Glaucoma in Diabetes Mellitus
- ▶ Ocular Prostheses
- ▶ Retinal Detachment
- ▶ Retinoblastoma
- ▶ Retinopathy of Prematurity
- ▶ Ruptured Globe
- ▶ Secondary Glaucoma in Uveitis

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Ephelides

- ▶ Ephelis (Freckle), of the Eyelid

Ephelis

- ▶ Ephelis (Freckle), of the Eyelid

Ephelis (Freckle), Conjunctival Disease

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Synonyms

Benign epithelial melanosis; Complexion-associated melanosis; Freckle

Definition

An ephelis (freckle) is a benign conjunctival epithelial hyperpigmentation characterized by an increase of melanin in the basal keratinocytes, and no melanocytic hyperplasia is present.

Etiology

The etiology of complexion-associated melanosis remains unclear, but available data suggests it may vary according to the skin pigmentation. It is considered to be a normal phenomenon in heavily pigmented individuals, whereas in light skin population, it can be considered abnormal. Chronic sun exposure could also be related to the development of this entity. This condition can also be congenital in nature.

Clinical Presentation

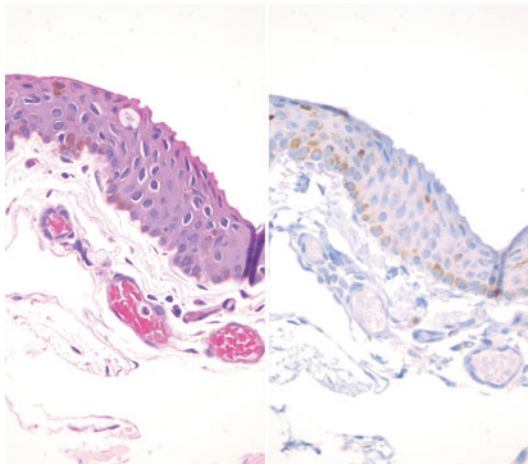
Ephelis appears at an early age. Usually, it is an asymptomatic, flat, brown patch with circumscribed pigmentation, occurring mainly at the perilimbal area. It fans out to lighter color, at the periphery, toward the fornix.

Diagnosis

Histopathological evaluation shows increased pigmentation of the epithelial basal layer and normal melanocytes (Fig. 1). There are no cytological atypia, nested pattern, or increase in number of melanocytes.

Differential Diagnosis

1. Nevus
2. Ocular melanocytosis
3. Primary acquired melanosis without atypia or benign acquired melanosis
4. Primary acquired melanosis with atypia
5. Melanoma



Ephelis (Freckle), Conjunctival Disease, Fig. 1 Histopathological finding

The ephelis or freckle is clinically and histopathologically indistinguishable from benign acquired melanosis.

Therapy

In general, ephelis does not require treatment if recognized in the appropriate setting. However, few cases may be somehow confusing because of the degree of pigmentation or increased growth and require biopsy.

Prognosis

Ephelis is benign and is not a precursor of malignant melanoma.

Epidemiology

It is more common in dark-skinned individuals.

Further Reading

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Ephelis (Freckle), of the Eyelid

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Synonyms

Ephelides; Ephelis; Freckle

Definition

A tan, flat macule on sun-exposed skin.

Etiology

Ephelides are a result of hyperpigmentation of the basal layer of the epidermis. The number of melanocytes is not increased, but melanin production is increased in the basal keratinocytes. Freckles tend to be inherited as an autosomal dominant trait and related to sun exposure (Albert and Jakobiec 2008).

Clinical Presentation

Ephelides are small circumscribed macules with uniform pigmentation on sun-exposed areas, occasionally on the eyelids or conjunctiva. Ephelides present during childhood and increase

in size and number in the summer months and lighten in the winter months (Albert and Jakobiec 2008).

Diagnostics

Excisional biopsy in not necessary but may provide definitive diagnosis in questionable cases. The number of melanocytes of the epidermis is not increased, but the melanosomes are larger.

Differential Diagnosis

Lentigo simplex
Lentigo, senile
Nevus, melanocytic
Malignant melanoma

Prophylaxis

Avoidance of sun exposure and sunscreens may prevent increased pigmentation.

Therapy

Treatment is not necessary. Chemical peels, cryotherapy, and laser treatments can be used to make the ephelides less pronounced.

Prognosis

Excellent. Patients in the same demographic tend to be more susceptible to skin cancers, so routine skin examinations are encouraged.

Epidemiology

Common and can be found on most individuals in varying degrees. They tend to be more pronounced in temperate climates.

Cross-References

▶ Lentigo Simplex (Simple Lentigines)
▶ Simple Lentigo

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Epibulbar Cancer

▶ Epibulbar Tumor

Epibulbar Choristoma

▶ Epibulbar Tumor

Epibulbar Dermoid

▶ Epibulbar Tumor

Epibulbar Dermolipoma

▶ Epibulbar Tumor

Epibulbar Melanoma

▶ Epibulbar Tumor

Epibulbar Osseous Choristoma

▶ Choristomas

Epibulbar Tumor

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Synonyms

Conjunctival tumor; Epibulbar cancer; Epibulbar choristoma; Epibulbar dermoid; Epibulbar dermolipoma; Epibulbar melanoma; Limbal dermoid

Definition

Epibulbar tumors are neoplasms found on the surface of the eye that arise from the conjunctiva, the cornea, or the limbus. In adults, the most common epibulbar tumors are melanoma (malignant tumor of conjunctival melanocytes), lymphoma (most commonly conjunctival MALT), and squamous cell carcinoma (maligant tumor of conjunctiva with squamous cell differentiation). Choristomas, growth of normal tissue in an abnormal location, are the most common epibulbar tumors in children and include dermoids and dermolipomas. Additional pediatric tumors include papillomas (benign epithelial tumor), nevi (benign conjunctival melanocyte proliferation), and rhabdomyosarcoma (malignant tumor with skeletal muscle differentiation).

Cross-References

- ▶ Choristomas
- ▶ Conjunctival Melanoma
- ▶ Conjunctival Tumors
- ▶ Corneal Intraepithelial Neoplasia
- ▶ Lymphoma: Definition
- ▶ Papillomas, Conjunctival
- ▶ Squamous Cell Carcinoma of Eyelid

Epidemic Keratoconjunctivitis (EKC)

- ▶ Acute Hemorrhagic Conjunctivitis

Epidermal Cyst

- ▶ Epidermal Cysts, of the Eyelid

Epidermal Cysts, of the Eyelid

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Synonyms

Epidermal cyst; Epidermal inclusion cyst; Milia; Molluscum contagiosum; Pilar cyst; Sebaceous cyst; Trichilemmal cyst; Xanthelasma

Definition

Benign, fluid-filled lesions affecting the superficial layers of the skin. Varieties include epidermal inclusion cysts, milia, molluscum contagiousum, pilar or trichilemmal cysts, and xanthelasma (Shields and Shields 1999; Albert and Jakobiec 2008).

Characteristics

Epidermal inclusion cysts are the most common epidermal cysts. They are slow-growing, solitary, round, smooth, elevated lesions with a surface layer of epidermis that tend to occur on the face, scalp, neck, and trunk. They frequently occur on the upper eyelids. They are thought to originate from occluded pilosebaceous follicles or surface

epidermis. Rupture of the cyst wall may cause a foreign body granulomatous reaction, and infection may lead to abscess formation. Treatment of choice is surgical excision.

Milia are multiple small umbilicated firm lesions that occur spontaneously or arise after trauma, radiation, or a herpes zoster infection. They are common in newborn infants. They are thought to be follicular retention cysts caused by the blockage of pilosebaceous follicles. Surgical excision is the treatment of choice or treatment with retinoic acid cream for multiple lesions.

Pilar or trichilemmal cysts occur in areas containing hair follicles, occasionally found in the eyebrow region. The cysts are filled with desquamated epithelium and can demonstrate calcification.

Molluscum contagiosum is a viral infection from the DNA poxvirus and can involve the eyelid margin. Typical lesions are characterized by a waxy nodule with central umbilication. They may be associated with a follicular conjunctivitis. Transmission in children can occur by direct contact or fomites, and sexual transmission is more common in adults. Numerous exuberant lesions may present in patients with acquired immunodeficiency syndrome. Treatment involves observation, excision, cryotherapy, or curettage. Topical or intravenous cidofovir may be required in immunosuppressed individuals.

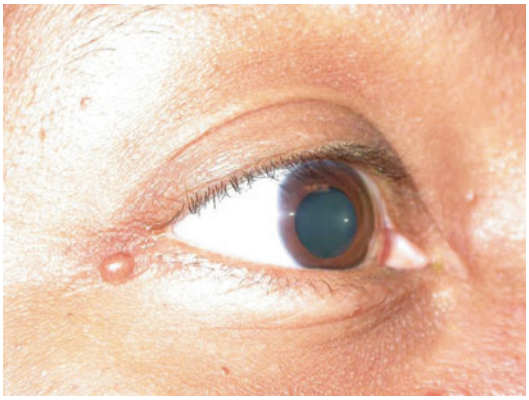
Xanthelasma are yellowish plaques in the inner medial canthal regions of the upper and lower eyelids. Lesions involve lipid-laden macrophages in the dermis and subdermal tissues. They can occur in patients with normal serum cholesterol but may be associated with systemic hypercholesterolemia and lipid disorders. Treatments include surgical excision and laser ablation (Shields and Shields 1999; Albert and Jakobiec 2008).

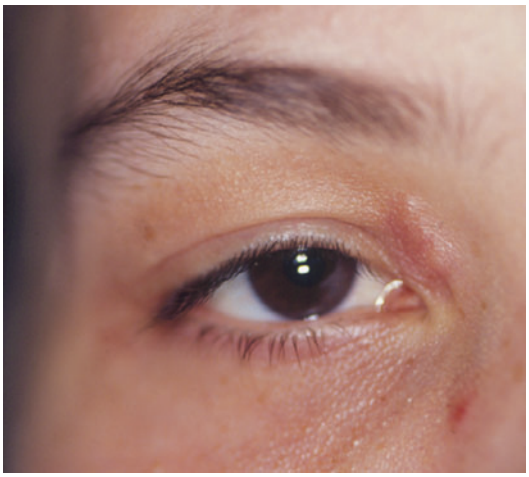
Differential Diagnosis

Epidermal inclusion cyst
Sebaceous cyst
Milia
Pilar cyst
Molluscum contagiosum
Xanthelasma

Management

See individual entities for further information.





Cross-References

- Epidermal Inclusion Cyst
- Milia
- Molluscum Contagiosum
- Pilar Cyst
- Sebaceous Cyst
- Trichilemmal Cyst
- Xanthelasma

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Epidermal Inclusion Cyst

▶ Epidermal Cysts, of the Eyelid
▶ Epithelial Inclusion Cysts

Epidermis

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Synonyms

Skin

Definition

The epidermis is a cutaneous structure characterized by stratified squamous epithelium that covers the external surface of the body (Weedon 2009).

Structure

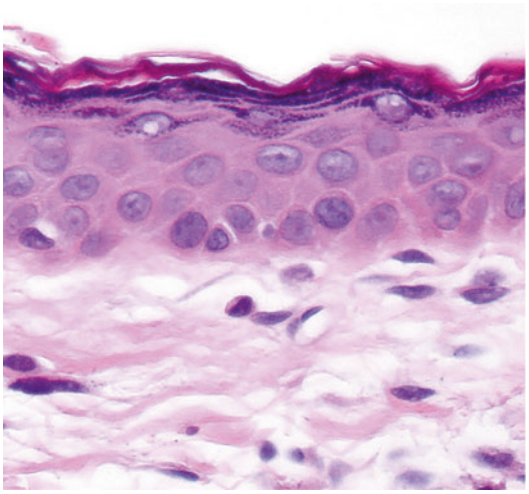
The skin is composed of keratinocytes and melanocytes forming a binary system (Javier and Ackerman 2001). The squamous epithelial cells (keratinocytes) are continuously regenerating with the cells undergoing terminal differentiation and death. Epidermal folds (*rete ridges*) invaginate into the dermis, while the latter one projects upward in between these ridges, forming the *dermal papilla.* The epidermis is separated from the dermis by a basement membrane, a complex, multilayered structure that gives rise to the epidermis structure (Haake and Polakowska 1993). The *basal layer* rests on the basement membrane, and it has the proliferating cells of the epidermis. Only around 17% of the basal cell population divides. These cells leave the layer to undergo terminal differentiation, while some immediately die by apoptosis due to intrinsic program or imbalance of signaling factors (McGowan and Coulombe 2000). Cells that enter the *prickle cell layer* which is four to ten cells thick are destined to differentiate; they acquire more cytoplasm and well-formed keratin filaments which are essential for the epithelial cells to tolerate stress (McGowan and Coulombe 2000). The desmosomes, prickles or intercellular attachments, develop here. As the cells are migrating toward the outer surface, they produce keratohyalin granules, forming the *granular layer* which is one to three cells thick. These cells lose their organelles and, subsequently, their function. They become flattened and form a dense, compacted keratinous layer known as *stratum corneum*. Finally, the superficial flake-like layer desquamates.

Function

The skin is now well known to be more than a protective and mechanical barrier. The keratinocytes in addition to the production of keratin are responsible for the biosynthesis of cytokines. Melanocytes produce a brown pigment (melanin) that represents an important endogenous protector against harmful UV sunlight. Langerhans cells are the epidermal dendritic cells that process and present antigens to lymphoid cells. Although Merkel cell function remains unclear, they reside within the basal layer and may serve mechanoreceptors or provide some sort of neuroendocrine function to the skin (Kumar et al. 2005).

Clinical Relevance

Several triggers such as UV light, stress, trauma, and surgery may affect the skin homeostasis and result in clinical conditions including wrinkles and hair loss, blisters and rashes, and life-threatening cancers and disorders of immune regulation. For example, chronic sun exposure may predispose to the development of a variety of



Epidermis, Fig. 1 Histological section of epidermis, H&E 400X

premalignant and malignant cutaneous neoplasms. Therapy with certain medications can also present with skin manifestations such rash or exanthemas, secondary to toxicity. Lastly, systemic and immune-related diseases including diabetes mellitus, lupus erythematosus, and amyloidosis, among others, may also have important manifestations in the skin (Kumar et al. 2005) (Fig. 1).

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Epidermoid Carcinoma

► Squamous Cell Carcinoma of Eyelid

Epidermoid Cysts

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Synonyms

Choristoma

Definition

These lesions are etiologically choristomas, i.e., masses of histologically normal-appearing tissue in an abnormal location. They are the most common epibulbar and orbital tumors in children, but may present at any age (Shields et al. 1984, 2004). They are formed during development as the suture lines of the skull close, during which time dermal or epidermal tissue may be pinched off to form cysts. They may displace structures in the globe and cause visual impairment due to optic nerve compression or restricting ocular motility (Cavazza et al. 2011).

Cross-References

► Choristomas
► Epibulbar Tumor

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Epiphora

▶ Tearing (Epiphora)

Epiretinal Membrane

▶ Cellophane Maculopathy

Episcleral Anesthesia

▶ Subtenon's Anesthesia

Episcleritis: Overview

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Definition

Episcleritis is inflammation of the tissue between the conjunctiva and sclera.

Etiology

Episcleritis is largely idiopathic. Collagen vascular disease, vasculitis, rosacea, atopy, herpes simplex, herpes zoster, gout, keratoconjunctivitis sicca, and atopic keratoconjunctivitis hold associations with episcleritis (Goldstein and Tessler 2009; Pearlstein 2011). One-third of cases are associated with an underlying disease (Goldstein and Tessler 2009). It may also follow administration of certain drugs like erlotinib, pamidronate disodium, risedronate, and topiramate (Pearlstein 2011).

Clinical Presentation

Episcleritis is a harmless and benign condition that presents acutely. Many individuals are asymptomatic, but some do experience minor discomfort and in rare cases severe pain (Goldstein and Tessler 2009; Pearlstein 2011). In cases of severe pain, it is more likely scleritis than episcleritis. Visual acuity is unaffected by this condition (Pearlstein 2011). Discharge may or may not be present, but when present is only watery (Pearlstein 2011). Purulent or mucopurulent discharge is not associated with episcleritis. Episcleritis should not be misunderstood as a mild form of scleritis.

The inflammation can be localized to the episclera by the vascular pattern. The episclera vascular plexus is straight and radial. The conjunctiva and sclera are freely anastomosing, and the conjunctiva plexus is mobile when moving the conjunctiva (Kanski and Bowling 2011; Pearlstein 2011). Another way to distinguish the condition is to give 2.5% phenylephrine, which blanches the conjunctiva vasculature. Ten percent phenylephrine can be used also, which will blanch the conjunctiva and superficial episcleral capillary plexus and leaves the deep vasculature alone that is inflamed in cases of scleritis. It may be beneficial to use red-free light when observing the vascular plexus pattern (Pearlstein 2011).

There are two presenting forms of episcleritis: simple and nodular. The simple form shows sectoral or diffuse redness from vascular congestion often in an interpalpebral distribution. This further distinguishes episcleritis from scleritis, as scleritis often has upper temporal quadrant distribution (Kanski and Bowling 2011). In 67% of cases, the inflammation will be sectoral and 33% will have diffuse inflammation (Pearlstein 2011). Episcleritis typically peaks in <12 h and then will slowly self-resolve over 6–10 days.

The nodular form of episcleritis presents one or more nodules in addition to simple episcleritis findings. These nodules are tender and in some cases can be found in the interpalpebral fissure (Kanski and Bowling 2011). These nodules can be differentiated from scleritis nodules by narrow,

bright slit beams. The episcleritis nodules will show the outer reflection displaced, while the inner reflection on the sclera and visceral episclera will be undisturbed (Pearlstein 2011). Scleritis nodules will show both inner and outer reflections as displaced (Pearlstein 2011). These nodules are also not phlyctenule, which are mobile as part of the conjunctiva (Goldstein and Tessler 2009).

Diagnosis

No laboratory diagnostics are available.

Differential Diagnosis

- Scleritis
- Conjunctivitis
- Phlyctenular conjunctivitis

Prophylaxis

Most cases are idiopathic. Control of underlying systemic or ocular disease is important.

Therapy

There is typically no intervention needed for episcleritis. In some cases, episcleritis presents with systemic diseases, and those systemic diseases should be treated as needed. Patients can be advised that cold compresses and cold artificial tears may help relieve symptoms. In severe cases, a systemic oral NSAID like flurbiprofen 100 mg three times daily may be used (Goldstein and Tessler 2009; Pearlstein 2011). In prescribing NSAIDs, it is not known if therapy should stop after symptoms resolve or to continue on afterward. Corticosteroid use is not recommended as these can lead to rebound episodes with more intense episcleritis with each recurrence (Goldstein and Tessler 2009; Pearlstein 2011).

Prognosis

Episcleritis typically resolves spontaneously. The peak occurs <12 h after onset and will improve over 5–10 days to where it will be completely resolved in 2–3 weeks (Goldstein and Tessler 2009; Kanski and Bowling 2011; Pearlstein 2011). Nodules will also resolve, but may take up to 4–5 weeks (Goldstein and Tessler 2009; Pearlstein 2011). Recurrence is a concern as 60% will recur around 2 months later and will continue in this pattern for 3–6 years (Pearlstein 2011). In some reported cases, these recurrent attacks have occurred for up to 30 years (Watson 2008). When associated with systemic disease, the recurrence is often delayed and at random intervals (Pearlstein 2011). Recurrence may lead to the random array and random sizes of the episclera tissue to rearrange into a more ordered pattern. This may cause the blue color of the uveal tissue to be seen, but does not represent scleral thinning (Pearlstein 2011). Otherwise, the structure of the eye is not damaged (Watson 2008). Complications are uncommon, but can include mild anterior uveitis, transient peripheral corneal infiltrates, and corneal dellen.

Epidemiology

The prevalence of episcleritis is not well known since most patients do not seek treatment since episcleritis is benign and resolves quickly. It is believed that 0.08% of hospital visits are due to episcleritis (Pearlstein 2011). Some studies have shown no association with gender, while some cite higher risk in females (Kanski and Bowling 2011; Pearlstein 2011).

Cross-References

▶ Conjunctivitis
▶ Necrotizing Scleritis
▶ Phlyctenules

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Episodic Anisocoria

► Benign Episodic Pupillary Mydriasis

Epithelial Abrasion

► Epithelial Defects

Epithelial Basement Membrane Dystrophy

► Map-Dot-Fingerprint Dystrophy (Epithelial/Anterior Membrane Dystrophy)

Epithelial Basement Membrane Dystrophy (EBMD)

► Corneal Dystrophies
► Epithelial Dystrophies

Epithelial Cyst

► Epithelial Inclusion Cysts

Epithelial Defects

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Synonyms

Corneal abrasion; Corneal defect; Corneal erosion; Epithelial abrasion; Epithelial erosion

Definition

Focal area of epithelial (outermost corneal layer) loss; can be due to mechanical trauma, corneal dryness, neurotrophic cornea, postsurgical changes, or any other of a variety of etiologies

Etiology

Corneal epithelial defects are one of the most commonly seen ocular pathologies in the general patient population (Reidy 2013–2014). Corneal epithelial defects are a focal loss of the corneal epithelium and can occur by a variety of means:

- Mechanical trauma (e.g., fingernail scratch, contact lens overuse, foreign body in the lid/fornices, trichiasis/distichiasis, chemical exposure)
- Exposure (e.g., neurotrophic diseases causing incomplete lid closure (commonly cranial nerve seven palsy), restrictive eyelid diseases, proptosis, decreased consciousness in drug abuse or comatose state, blepharoplasty, lagophthalmos)
- Ultraviolet burns (e.g., welding, prolonged sun exposure off reflective surfaces)
- Local corneal dryness and systemic disorders leading to corneal dryness (e.g., dry eye syndrome, thyroid eye disease, Sjogren's syndrome, vitamin A deficiency)
- Limbal stem cell deficiency (failure to regenerate epithelial cells, occurs from a variety of causes, e.g., chemical burns, postocular surgery, ocular autoimmune degenerations)

- Topical anesthetic abuse
- Neurotrophic keratopathy (corneal hypoesthesia or anesthesia caused, most frequently, by damage to the trigeminal nerve, also HSV, VZV, and topical drop toxicity, among others (Wilson 2009))

Corneal defects are frequently accompanied by pain, tearing, and foreign body sensation of the affected eye (the exception being neurotrophic keratopathy) which are commonly alleviated by the instillation of topical anesthetic. They can also be accompanied by photophobia, pain with blinking and pain with eye movement. Conjunctival injection is frequently present on the ipsilateral side of the corneal defect. Periorbital skin or lid changes are present variably given the etiology of the defect (e.g., skin burns with chemical exposures, periorbital trauma in post-motor vehicle collision defects, poor lid closure in exposure defects).

When visualizing corneal defects, fluorescein dye is instilled either as a liquid drop (mixed with a topical anesthetic) or via a fluorescein impregnated paper strip after the instillation of topical anesthetic. The dye is visualized using a cobalt-blue filter which causes the dye to fluoresce a bright green color. Fluorescein does not stain intact corneal epithelium but does stain corneal stroma, thus demarcating the area of the epithelial loss. The distribution, size, and shape of the corneal defect will vary depending on the etiology (e.g., thin, linear defect for fingernail scratch, whole corneal surface defect for an extensive chemical burn, inferior corneal irregular defect for lid abnormalities/lagophthalmos).

A thorough history is required to determine the etiology of the corneal defect. Similarly, a thorough exam of both eyes is needed because in many cases of systemic diseases or trauma, both eyes can be affected.

Occurrence

Corneal epithelial defects accounted for 10% of all eye-related emergency room visits in the early 1990s (Shields and Sloane 1991). They are a common, and frequently overlooked, ocular pathology. Specific occurrences vary by etiology of epithelial defect.

Classification

Corneal disease, corneal trauma

Cross-References

- ▶ Chemical Injury (Burns)
- ▶ Epithelial Erosions
- ▶ Exposure Keratitis/Keratopathy
- ▶ Exposure Staining, Keratoconjunctivitis Sicca
- ▶ Lagophthalmos
- ▶ Limbal Stem Cells
- ▶ Punctate Epithelial Defects/Erosions
- ▶ Superior Limbic Keratoconjunctivitis
- ▶ Trichiasis

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Epithelial Dystrophies

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Synonyms

Anterior corneal dystrophies; Epithelial basement membrane dystrophy (EBMD); Lisch epithelial corneal dystrophy; Meesman's epithelial dystrophy

Definition

Epithelial dystrophy is a bilateral disease that affects the outermost layer of the cornea and is characterized by intraepithelial cysts and

abnormal basement membrane, leading to recurrent epithelial erosions, which can be painful and cause blurred vision. There are three subtypes of epithelial dystrophy including EBMD which is the most common anterior corneal dystrophy seen by the comprehensive ophthalmologist, Meesman's epithelial dystrophy, and the Lisch epithelial corneal dystrophy. EBMD is often sporadic but may be inherited in an autosomal dominant fashion; point mutations in the TGFB1 gene have been associated in a minority of cases.

Further Reading

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Epithelial Edema

► Bulla

Epithelial Erosion

► Epithelial Defects

Epithelial Erosions

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Synonyms

Corneal abrasion; Corneal erosion; Recurrent corneal erosion

Definition

Epithelial erosion is the detachment of the outermost corneal epithelial cells from the underlying Bowman's layer. It occurs as a result of corneal trauma, dystophy, or disease. The primary symptom of erosion is pain, as the loss of surface epithelium exposes sensory nerve fibers (ciliary nerves from the ophthalmic division of the trigeminal nerve). Other symptoms include foreign body sensation, photophobia, and blurred vision. Recurrent corneal erosion refers to repeated episodes of epithelial erosion.

Cross-References

► Corneal Abrasion
► Epithelial Defects
► Punctate Epithelial Defects/Erosions
► Recurrent Corneal Erosion
► Stromal Micropuncture, for Recurrent Corneal Erosions

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Epithelial Inclusion Cysts

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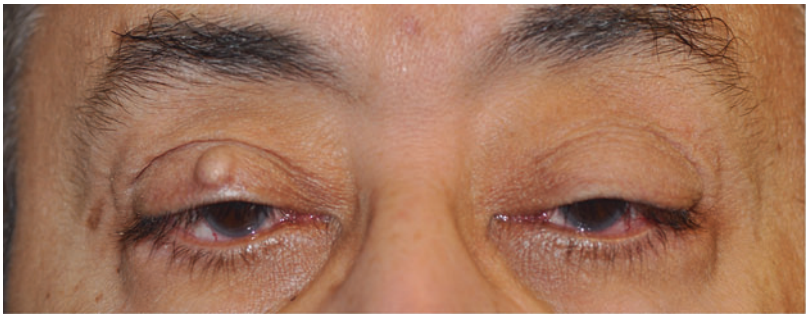
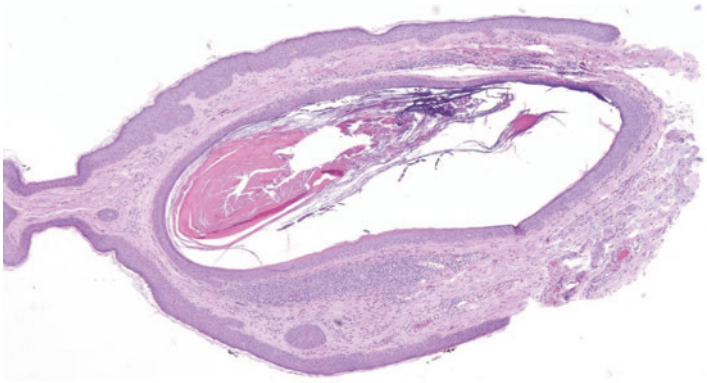
Synonyms

Epidermal inclusion cyst; Epithelial cyst



Epithelial Inclusion Cysts, Fig. 1 Epithelial Inclusion Cyst, right upper lid (RUL). Courtesy: Roxana Rivera-Michilig, MD



Epithelial Inclusion Cysts, Fig. 2 Epithelial Inclusion Cyst, H&E 40X Courtesy: Michael Mines, MD

Definition

Epidermoid cyst is a benign, slow-growing, round, firm, subcutaneous tumor lesion that can be congenital or secondary to trauma or surgery (Shields and Shields 2008; Kronis et al. 1988). It tends to occur at the outer upper portion of the upper eyelid and also in the superotemporal region of the orbit. They are filled with cheesy, foul-smelling keratin debris and lined by keratinizing stratified squamous epithelium that resembles normal epidermis (Figs. 1 and 2) (Yanoff and Sassani 2009; Eagle 2011).

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Epithelial Microcystic Edema

► Microcystic Epitheliopathy

Epithelial Reinforcement Technique

► Stromal Micropuncture, for Recurrent Corneal Erosions

Epithelioma Contagiosum

► Molluscum Contagiosum, of Eyelid
► Molluscum Contagiosum: Overview

Epitheliopathy

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Definition

Epitheliopathy refers to any disease that affects the epithelial cells of the eye. The cornea, conjunctiva, ciliary bodies, iris, lens, and retina all contain epithelial cells and may be affected by disease or disorder. Due to its location, the cornea is the most susceptible to insults that may result in epitheliopathy.

Cross-References

- ▶ Corneal Dystrophies
- ▶ Epithelial Defects
- ▶ Epithelial Dystrophies
- ▶ Epithelial Erosions
- ▶ Epithelial Inclusion Cysts
- ▶ Gardner Syndrome: Retinal Pigment Epithelium Hypertrophy
- ▶ Juvenile Epithelial Dystrophy (Meesmann Dystrophy)
- ▶ Keratitis
- ▶ Keratoconjunctivitis Sicca
- ▶ Lens Epithelial Cells
- ▶ Map-Dot-Fingerprint Dystrophy (Epithelial/Anterior Membrane Dystrophy)
- ▶ Pigment Epithelium, Ciliary Body, and Iris
- ▶ Sattler's Veil (Central Epithelial Edema)

Eruptive Hemangioma

- ▶ Pyogenic Granuloma

Erythema Multiforme Major

- ▶ Stevens Johnson Syndrome

Erythrocyte Sedimentation Rate in Giant Cell Arteritis

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Synonyms

ESR; Sed rate

Definition

An erythrocyte sedimentation rate (ESR) is a hematology test that is a nonspecific indicator of inflammation. The ESR can be used to diagnose or to monitor the course of treatment in inflammatory disease. In healthy blood, sedimentation of erythrocytes (erythrocytes gradually separate from plasma and settle to the bottom of a container) occurs slowly (due to negative surface change), while during inflammatory disease, the rate of sedimentation is more rapid. ESR is measured as a rate (distance in millimeters that erythrocytes have fallen from the plasma meniscus over time defined in mm per hour).

Giant cell arteritis (GCA, also known as temporal arteritis) is typically associated with

elevated ESR. An ESR is usually measured by the Westergren method. It is considered to be elevated if above 40 mm/h and is elevated in up to 85% of patients with GCA. Age increases the ESR however and one empiric calculation of normal is age and gender based. For men, age divided by 2 and for women age +10 divided by 2 are common empiric formulas for defining normal. An elevated ESR however is nonspecific and can be seen in other conditions that may involve changes in plasma proteins such as rheumatic fever, hypercholesterolemia, rheumatoid arthritis, lupus, anemia, macrocytosis, inflammatory disease, viral hepatitis, tuberculosis, cancer, multiple myeloma, increased plasma fibrinogen, and increased plasma globulins. A decreased sedimentation rate, on the other hand, could indicate the presence of sickle cells, microcytosis, increased plasma viscosity, spherocytosis, or polycythemia.

Cross-References

▶ Giant Cell Arteritis

Further Reading

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Eskimo Corneal Degeneration

▶ Keratinoid (Spheroidal) Degeneration
▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
▶ Spheroidal Degeneration

ESR

▶ Erythrocyte Sedimentation Rate in Giant Cell Arteritis

Essential Anisocoria

▶ Physiologic Anisocoria

ETDRS

▶ Early Treatment Diabetic Retinopathy Study (ETDRS)

ETDRS Chart

▶ ETDRS Visual Acuity Chart

ETDRS Visual Acuity Chart

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Synonyms

ETDRS chart

Definition

The ETDRS chart has been introduced as a standardized visual acuity (VA) testing chart for the ▶ Early Treatment of Diabetic Retinopathy Study (ETDRS). It uses 14 lines of 5 ▶ Sloan letter optotypes in each line in logarithmic progression. The space between lines and letters is proportionally equal keeping the effect of contour interaction constant. The threshold VA corresponds to the line in which 3 out of 5 optotypes were correctly identified. Alternatively, a by-letter scoring system (−0.02 logMAR credited for each letter correctly read) can be used. The testing distance can be varied; the corresponding visual acuity can be read easily from the chart. The chart is mounted on a box that is backlit by fluorescent tubes. For repeated measurements, the chart itself can be exchanged, providing different letters for different eyes.

Its easy design, its high standardization (logarithmic progression, backlit box), and the opportunity of

using the chart at different distances – especially at a short distance for low-vision testing – have established the ETDRS chart as the standard chart for testing visual acuity. In particular, shortcomings of its predecessor the traditional ▶ Snellen chart such as unequal design of the different lines and non-logarithmic progression were overcome.

Cross-References

▶ Minimum Angle of Resolution/Recognition (MAR)
▶ Sloan Letters

Everting Sutures

▶ Sutures (Surgical), Quickert, for Involutional Entropion

Evisceration

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Definition

Evisceration involves the removal of the internal contents of the eyeball, leaving the sclera, extraocular muscles, and optic nerve intact (2008).

Indications

There are several indications for evisceration. The most common are as follows:

1. Blind painful eye
2. Suppurative endophthalmitis

Blind Painful Eye

There are numerous causes of a blind painful eye. Trauma, neovascular glaucoma, chronic retinal detachment, chronic angle closure glaucoma, retinopathy of prematurity, uveitis, and tumors can all lead to a blind painful eye. When conservative measures such as topical medications, cyclodestructive therapy, or retrobulbar injection of alcohol or thorazine have failed to control the pain, removal of the eye must be considered. Enucleation and evisceration can both be reasonable options and should be chosen based on the surgical goals of the patient and surgeon. Evisceration holds several advantages over enucleation:

1. There is less disruption of orbital anatomy.
2. Potential for better motility of the prosthesis.
3. Less-invasive procedure better tolerated by those with significant comorbidities.
4. Superior treatment for endophthalmitis.

Suppurative Endophthalmitis

In suppurative endophthalmitis, evisceration is commonly used over enucleation as removal of the ocular contents, and therefore, by definition, the infection can be undertaken without invasion of the orbit. As a result, the risk for spread of infection to the orbit or intracranial space is reduced.

Contraindications

Evisceration has several contraindications as well as known disadvantages to enucleation. First and most importantly, any potential for or known presence of intraocular tumor is an absolute contraindication to evisceration. If removal of the eye is indicated in these cases, enucleation must be done to ensure complete removal of the mass (if possible) and also provide for a complete specimen for pathologic evaluation.

Another important contraindication is the risk of sympathetic ophthalmia. This rare form of granulomatous uveitis can cause severe visual loss in the fellow or "sympathizing" eye. Eyes indicated for removal after penetrating trauma or multiple surgical procedures theoretically have an increased risk of sympathetic ophthalmia and

should undergo enucleation rather than evisceration. It is currently recommended that enucleation be carried out within two weeks of the trauma to help reduce the likelihood of sympathetic ophthalmia. Although there is a perceived advantage of enucleation over evisceration for prevention of sympathetic ophthalmia, this has never been proven (Moshfeghi et al. 2000).

Lastly, the shape of the eye needs to be taken into consideration prior to surgery. Eyes that are phthisical or have undergone scleral buckling, for example, are poor candidates for evisceration. The procedure itself and implant placement can be very difficult in these cases.

Techniques and Principles

Evisceration is usually carried out under general anesthesia; however, retrobulbar infusion of local anesthetic and monitored anesthesia care (MAC) can be used. Evisceration can be performed with or without keratectomy. The ocular contents are removed completely leaving bare sclera and overlying conjunctiva. An implant of sufficient volume is centered within the globe. The globe is then closed. A conformer can be placed to retain the anatomy of the fornices if needed. In cases of endophthalmitis, some surgeons will avoid placement of an implant given the setting of active infection (Stewart 1995).

Outcomes

The goal of evisceration is to remove the source of ocular pathology while delivering an acceptable cosmetic outcome. A prosthesis is placed in addition to the implant after adequate healing time to achieve good motility, normal eyelid shape and position, as well as normal volume and surface appearance.

Complications

Complications can occur intraoperatively and postoperatively. Intraoperative complications include evisceration of the wrong eye, orbital hemorrhage, and difficulty with intrascleral implant placement. Postoperatively, hemorrhage, edema, and infection can complicate the early course, while enophthalmos, superior sulcus deformity, and implant exposure and extrusion can occur months to years after the initial surgery. Most importantly, as mentioned above, the risks of undiagnosed intraocular tumor and of postoperative sympathetic ophthalmia are rare but potentially devastating complications.

Cross-References

- ▶ Angle-Closure Glaucoma
- ▶ Enucleation
- ▶ Neovascular Glaucoma in Diabetes Mellitus
- ▶ Retinal Detachment
- ▶ Retinopathy of Prematurity
- ▶ Secondary Glaucoma in Uveitis

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Excimer Laser Photoablation

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Synonyms

Exciplex laser photoablation

Definition

Removal of corneal tissue using an excimer laser that emits very concentrated light in the ultraviolet (UV) region of the spectrum (193 nm) (Azar 2007).

Epidemiology

Worldwide an estimated number of over 30 million corneal excimer laser photoablations are performed each year. Around 95% are laser in situ keratomileusis (LASIK) procedures and 5% are advanced surface ablations (ASA).

History

Laser vision correction has grown with tremendous speed over the years since the first applications on human corneas in the 1990s. In addition to the choice of ASA or lamellar treatments like LASIK, the surgeon now has to select a laser profile for myopic, hyperopic, or astigmatic treatment. Wavefront-guided, wavefront-optimized (aspheric), and topography-guided ablation are the most advanced and frequently used profiles in current practice (Kohnen et al. 2007).

Clinical Features

Standard or planoscan treatment profile has been used for many years and produces very predictable results. The nature of the corneal reshaping, however, can lead to the induction of other complex optical aberrations after this type of ablation. Therefore, patients with higher optical errors, larger pupils, or with preexisting higher optical aberrations (HOA) may be better suited to another treatment profile.

Aspheric treatment profile is based on subjective refraction and corneal topography. It incorporates some elements of wavefront-guided treatment. The essential advantage is that the corneal reshaping is done in a more selective way resulting in excellent optical correction but without inducing spherical aberration. By not inducing this particular aberration, patients achieve better mesopic visual performance. This treatment profile is an option for patients with larger pupil size in dim light in the presence of minimal preexisting higher order aberrations and also for patients who have higher degrees of pre existing spherical aberration without substantial amounts of other HOA.

Wavefront-guided treatment profile is sometimes referred to as personalized or customized treatment profile. Assessment of the corneal wavefront is based on the principle that if an eye had no imperfections at all, a single point of light passing to the retina would not scatter and be seen as a tiny single point of light at the retina. But as no optical system is perfect, some individual light scattering occurs in every eye. A wavefront-guided treatment profile is able to correct HOA and is an option for patients with larger pupil size and marked HOA.

Topography-guided treatment profile or TopoLink profile is also based on subjective refraction and corneal topography and is an option for patients with corneal irregularities or underlying irregular corneal astigmatism (Kohnen 2008).

Tests

In advance to every corneal photoablative surgery, the excimer laser energy level is tested into appropriate substrate materials, the so-called "fluence test." Laser fluence is a measure of the energy density and is described as the amount of energy applied per unit area with each single pulse in mJ/cm2. Minimum fluence required for proper ablation is approximately 50 mJ/cm^2.

Differential Diagnosis

Today, corneal photoablation is solely performed with the excimer laser.

Etiology

The term "photoablation" refers to the greek term "phos" (light) and the latin term "ablatio" (removal).

Treatment

Excimer laser corneal photoablation is approximately 0.3–0.5 μm per pulse. Using modern excimer lasers with high pulse frequencies, photoablation is performed in less than 60 s per eye even treating higher ametropias. Though the tissue immediately adjacent to the excimer laser photoablation pulse may increase in temperature to about 40°, modern flying spot lasers seem not to produce significant increase in surface temperatures.

Cross-References

- ▶ Excimer Lasers
- ▶ Higher-Order Aberrations, Refractive Surgery

References

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Excimer Laser Phototherapeutic Keratectomy

▶ Phototherapeutic Keratectomy

Excimer Lasers

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Synonyms

Exciplex laser

Definition

A gas LASER (light amplification by stimulated emission of radiation) in which a very short electrical pulse excites a mixture containing a halogen such as fluorine and a rare gas such as argon or krypton that emits very concentrated light in the ultraviolet (UV) region of the spectrum (193 nm). The term excimer is an acronym of "excited" and "dimer" with regard to the laser-active medium. A dimer is a molecule consisting of two identical atoms or molecules.

Epidemiology

Today, an estimated number of 5000–1,0000 excimer lasers are used worldwide for an estimated number of over 30 million refractive surgical procedures each year.

History

The first excimer laser was used in 1970 by N. Bassow, V. A. Danilychew, and Y. M. Popow at the P. N. Lebedew Physics Institute in Moscow, Russia. The first commercial excimer laser was

built in 1977 by Lambda Physics. In 1983, following initial reports by S. L. Trokel and R. Srinivasan that this laser could reshape the cornea without collateral thermal damage, animal experiments were pursued by M. B. McDonald, S. L. Trokel, and T. Seiler. The early excimer lasers were designed to perform slits in the cornea to simulate incisional surgery, but this was soon abandoned. After introduction of the Munnerlyn formula, photorefractive keratectomy (PRK) was introduced. This was followed by primate experiments and human clinical trials, ultimately gaining FDA approval of PRK for use on human eyes in 1995. LASIK (laser in situ keratomileusis) soon became the dominant procedure, and wave front technology and aspheric ablations led to customized treatments. Videokeratography, femtosecond laser-assisted flap creation, and advances in wave front technology played an important role in advancing the field resulting in its widespread worldwide acceptance today.

Clinical Features

Modern excimer lasers work with pulse frequencies of 100–1000 Hz and a spot diameter around 1 mm. An entire laser weights around 500–1000 kg, amount of space needed is around 4 × 4 m, and the minimum prize in $ is at least six digit.

Tests

Thorough examination of the eyes and workup of the patient's anamnesis is mandatory to rule out several exclusion criteria for excimer laser refractive surgery. See also chapters PRK, LASEK, and LASIK.

Differential Diagnosis

Other LASERs that are used for ophthalmic surgical procedures:

- Femtosecond laser
- Nd:YAG (neodymium-doped yttrium aluminum garnet) laser
- Argon laser
- Diode laser
- Carbon dioxide laser

Etiology

See "History" section above.

Treatment

Almost all types of corneal refractive procedures use an excimer laser. Some novel techniques like SMILE (small-incision *femtosecond* lenticule extraction) or FLEx (femtosecond lamellar extraction) work with femtosecond laser technology and do not implement an excimer laser for corneal ablation. For detailed illustration of the different surgical procedures, refer to chapters PRK, LASIK, Epi-LASIK, and LASEK.

Cross-References

- ▶ Excimer Laser Photoablation
- ▶ Femtosecond Laser
- ▶ Wavefront-Guided Laser Refractive Surgery

Further Reading

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Exciplex Laser

- ▶ Excimer Lasers

Exciplex Laser Photoablation

▶ Excimer Laser Photoablation

Excisional Biopsy

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Synonyms

Biopsy

Definition

Surgical removal of a lesion whereby the tumor is removed completely, utilizing an elliptical or other circumferential surgical pattern surrounding the lesion, in order to prevent recurrence or to avoid leaving any tumor behind.

Purpose

To fully remove a lesion in question to prevent recurrence or achieve cure or both. An excisional biopsy is also often used if a deep inflammatory lesion or malignancy is suspected.

Principle

First, the tissue surrounding the lesion is anesthetized with local anesthetic with epinephrine. A sharp incision is fashioned circumferentially around the lesion, usually with an eliptical pattern and preferably in relaxed skin tension lines. A rim of normal tissue, around 1–2 mm (more if the surgeon suspects an aggressive malignancy) is typically included to secure the diagnoses of clear margins. Including the adjacent normal tissue also aids in histopathologic characterization of the abnormal tissue (Nerad 2001; Albert and Jakobiec 2008).

Indication

A wide excisional biopsy is highly warranted in any lesion suspicious for malignancy, such as melanoma. Benign lesions with high recurrence rate also may warrant an excisional biopsy in order to prevent recurrence.

Contraindication

Lesions that can be removed with simpler techniques, such as a shave biopsy. Abnormal bleeding times, due to therapeutic or pathological causes, may also preclude safe excisional biopsy. An excisional biopsy may also be avoided if the lesion is intimately associated with vital structures and excision risks functional or structural damage.

Advantages/Disadvantages

Removal of the whole lesion may increase the likelihood of a complete cure and may eliminate the need for further surgery. Disadvantages of this type of biopsy include: possibly larger tissue area removal, potential for higher bleeding complications, possible structural or functional damage to the area, and a potential for an unacceptable cosmetic result if not performed properly (Nerad 2001; Albert and Jakobiec 2008).

Cross-References

▶ Choroidal and/or Ciliary Body and/or Iris Melanoma

References

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Exfoliative Glaucoma

► Pseudoexfoliative Glaucoma

Exophthalmos (When Associated with Thyroid Eye Disease)

► Proptosis

Exposure Keratitis/Keratopathy

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Synonyms

Lagophthalmic keratitis

Definition

Exposure keratopathy is a noninfectious inflammation of the cornea that results after incomplete lid closure or lagophthalmos (Kanski and Bowling 2011). The cornea remains unprotected from drying despite normal tear production.

Etiology

The most frequent cause of lagophthalmos associated with exposure keratopathy is facial nerve palsy (Kaiser and Friedman). Facial nerve palsy may be idiopathic or secondary to surgery for acoustic neuromas or parotid gland tumors. Lagophthalmos may also be caused by reduced muscle tone, as may be observed in comas. Nocturnal lagophthalmos is noted for some patients (Kanski and Bowling 2011). Mechanical trauma and burns may cause eyelid scarring, limiting eyelid closure. Increased skin tightness due to eczema, taut skin, solar keratosis, and even blepharoplasty may result in lagophthalmos. Globe position may also play a factor. The end result of persistent lagophthalmos is drying of the cornea and inflammation leading to exposure keratopathy.

Occurrence

Exposure keratitis can affect individuals of all ages and equally males and females. Of note, it has become a growing concern in ICU care. Some reports have revealed the incidence of exposure keratitis to range from 20% to 42%, ranging from 2 to7 days in the ICU setting (Rosenberg and Eisen 2008).

Classification

Exposure keratopathy is diagnosed in the absence of an infectious etiology (Kanski and Bowling 2011). Limited eyelid closure is associated with the disease. Patients will present with symptoms of dry eye, itching, burning, decreased vision, and foreign body sensation. Physical exam and slit lamp will reveal punctate epithelial changes, epithelial breakdown. Severe findings include stromal melting with possible corneal perforation and secondary infection.

The extent of disease guides the type of treatment that may be pursued. Reversible exposure may be treated with artificial tears during the day and ointment during the night (Kanski and Bowling 2011). Bandage silicone rubber or scleral contact lenses may be of aid to some patients. Temporary tarsorrhaphy or occlusive dressings may be necessary. In cases where permanent

exposure is of concern, permanent tarsorrhaphy is a treatment option. Alternative treatment methods include placement of gold weights into the upper lid (especially in cases with facial nerve palsy). Orbital involvement may necessitate orbital decompression.

Cross-References

- ▶ Infectious Keratitis with Ulceration
- ▶ Lagophthalmos
- ▶ Stromal Keratitis (Herpetic)
- ▶ Ulcerative Keratitis

References

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Exposure Staining, Keratoconjunctivitis Sicca

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Synonyms

Ocular surface staining

Definition

Exposure staining is defined as the use of dyes, like fluorescein, rose bengal, and lissamine green, to stain and identify damaged corneal and conjunctival epithelial cells (Holland et al. 2013).

Purpose

Keratoconjunctivitis sicca, or dry eye syndrome, may result in corneal and conjunctival epithelial cell damage (Kanksi and Bowling 2011). The use of ocular surface staining allows for identification of devitalized and desiccated corneal and conjunctival tissue under slit-lamp examination.

Principle

The principle of exposure staining is to visually identify extent of epithelial cell damage on examination. Fluorescein enters and dyes damaged corneal and conjunctival epithelial cells (Kanksi and Bowling 2011) Rose bengal is a dye that has a high affinity for injured or dead epithelial cells that have lost their protective mucous layer. Lissamine green has a similar staining pattern to rose bengal.

Indication

The pattern of staining may aid in the diagnosis and assessment of dry eye syndrome. Fluorescein staining has shown to be of use for staining of diseased cornea, while rose bengal and lissamine green have been more useful for staining diseased conjunctiva (Holland et al. 2013).

Patients presenting with symptoms of dry eyes (itching, burning, redness, decreased vision, foreign body sensation) necessitate a slit-lamp examination and ocular surface staining. Staining may reveal several findings. For example, interpalpebral staining of the cornea and conjunctiva is found during tear deficiency (Kanksi and Bowling 2011). A superior limbic keratoconjunctivitis may be indicated on a superior conjunctival stain. Inferior stains may rather hint exposure keratitis or blepharitis.

Contraindication

Ocular staining is well tolerated by patients, and there are no contraindications other than adverse reactions/stinging to the particular stain.

Advantage/Disadvantage

Ocular staining has several advantages for determining the extent of keratoconjunctivitis sicca. The greatest advantage is its low risk potential (Holland et al. 2013). Fluorescein staining is highly tolerable and does not cause stinging in the patient. However, it may stain contact lenses, and patients should be warned that their eyes may remain yellow for a short period of time. A disadvantage may also be that the fluorescein tear film may obscure accurate corneal staining measurements (Bron et al. 2003). Tear film assessments prior to application may improve staining measurements.

Rose bengal dye may cause stinging that can last up to a day. A topical anesthetic should be applied prior to its use (Holland et al. 2013).

Lissamine green, however, carries a similar staining profile as rose bengal and is not associated with stinging (Holland et al. 2013). It is better tolerated by patients and has grown in its popularity in clinical practice.

Cross-References

- ▶ Dry Eye
- ▶ Keratoconjunctivitis Sicca
- ▶ Schirmer Tests

References

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External Hordeolum (Stye)

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Synonyms

Stye

Definition

It is an acute bacterial infection resulting in a painful, nodular lesion on the external anterior eyelid.

Etiology

An external hordeolum is an acute bacterial infection of one or more sebaceous glands of Zeis or apocrine sweat glands of Moll. The most common cause is *Staphylococcus aureus*. Hordeolum is associated with chronic blepharitis, meibomian gland dysfunction, and acne.

Clinical Presentation

A hordeolum presents as an acute, painful, erythematous, subcutaneous, nodular abscess on the margin of the anterior eyelid. One or more lesions appear and can sometimes involve the entire lid margin. Swelling and crusting of the eyelid and mucopurulent discharge from the eye may be present. Symptoms include localized pain, tenderness, burning, irritation, blurred vision, photophobia, and tearing. Rarely, the infection may spread to adjacent tissue, secondarily causing preseptal cellulitis.

Diagnosis

Diagnosis is based on clinical appearance and symptoms. No additional tests are necessary for diagnosis.

Differential Diagnosis

It may be difficult to differentiate a hordeolum from an acute chalazion. However, a chronic chalazion will be firm and nontender, in contrast with a hordeolum, which is acute, painful, and self-limiting. Blepharitis and preseptal cellulitis should also be considered in the differential. With a history of recurrent hordeola, suspicion for neoplasm may be increased, particularly sebaceous gland carcinoma, basal cell carcinoma of the eyelid, and squamous cell carcinoma of the eyelid. Histopathologic examination of tissue will be able to differentiate between these neoplasm diagnoses (Weisenthal et al. 2013).

Prophylaxis

Proper daily eyelid hygiene with warm compresses can prevent the development of a hordeolum and minimize blepharitis and meibomian gland dysfunction, both of which are risk factors for hordeolum. Appropriate hand washing can decrease infection.

Therapy

The main medical management is eyelid hygiene. Warm compresses with gentle massage for at least 10 min, four times a day, can facilitate drainage and are generally sufficient for complete resolution. A hordeolum should not be forcefully ruptured to prevent further spread of the infection. Topical antibiotics usually are not effective but are prescribed if there is associated blepharoconjunctivitis. Systemic antibiotics are administered if there is secondary preseptal cellulitis. Treat concomitant blepharitis to minimize recurrence of hordeola. If there is no resolution with medical therapy, incision and drainage can be performed through the skin and orbicularis. A sample can be sent for histopathologic examination to rule out malignancy (Krachmer et al. 2011).

Prognosis

A hordeolum is usually self-limiting, resolving within 1–2 weeks. They may recur. Secondary complications, although rare, include preseptal cellulitis and a systemic infection.

Epidemiology

Hordeola are common, more so in adults compared to children. The incidence and prevalence are unknown. There does not appear to be a racial or gender predominance.

Cross-References

- ▶ Basal Cell Carcinoma of Eyelid
- ▶ Blepharitis
- ▶ Blepharoconjunctivitis
- ▶ Cellulitis, Preseptal, Haemophilus Causing
- ▶ Chalazion
- ▶ Glands of Krause, Glands of Moll, Glands of Wolfring, Glands of Zeis
- ▶ Meibomian Gland Dysfunction
- ▶ Sebaceous Gland Carcinoma
- ▶ Squamous Cell Carcinoma of Eyelid

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Extraconal Anesthesia

- ▶ Peribulbar Anesthesia

Extraperiosteal Route

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Synonyms

Subperiosteal orbitotomy

Definition

An orbitotomy designed to access the subperiosteal or extraperiosteal space of an orbital wall.

Indications

This is often performed for drainage of a subperiosteal abscess that may be continuous from the frontal, ethmoid, or maxillary sinus, for orbital fracture repair, or for bony decompression of the orbit.

Contraindication

Contraindications include need for access to lesions not in the subperiosteal space or for patients who are not medically stable for surgery.

Techniques and Principles

This procedure is generally performed in the operating room under sedation or general anesthesia. The subperiosteal space of the inferior and superior orbit may be accessed through a transcutaneous incision through the lower or upper eyelid, respectively. In the upper eyelid, the incision may go through the transeptal plane if necessary, or just superior to the septum, depending on the area of interest. A vertical eyelid splitting procedure may be used if a broader exposure is desired. The inferior extraperiosteal space may also be accessed through a lower eyelid transconjunctival approach. Medially, for drainage of a subperiosteal abscess from the ethmoids, fracture repair of the medial wall, or medial wall decompression, a transcaruncular or frontoethmoidal, or Lynch, incision may be taken to access this area (Cockerham et al. 2001; Levine 2003; Mohadjer and Hartstein 2006). The medial and inferior subperiosteal spaces may also be accessed endoscopically during sinus surgery for decompression or abscess drainage (Nerad 2001; Tsirbas et al. 2005). For lateral subperiosteal access, a lateral orbitotomy is performed (Cockerham et al. 2001; Levine 2003; Mohadjer and Hartstein 2006).

Outcome

Access to the subperiosteal spaces of each orbital wall for drainage of an abscess, bony decompression, or fracture repair.

Complications

Risks of extraperiosteal orbitotomy include risks associated with anesthesia, bleeding, pain, infection, scarring, swelling, loss of vision, damage to adjacent structures, diplopia, and need for additional procedures.

Cross-References

- ▶ Frontoethmoidal Incision, for Anterior Orbitotomy
- ▶ Graves Ophthalmopathy
- ▶ Lynch Incision, for Anterior Orbitotomy
- ▶ Orbit, Inflammation of
- ▶ Transcaruncular Route, for Anterior Orbitotomy
- ▶ Transconjunctival Route
- ▶ Transcutaneous Routes
- ▶ Vertical Eyelid Splitting, for Anterior Orbitotomy

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Eye Allergies

▶ Allergic Conjunctivitis

Eye Bank Association of America

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Synonyms

EBAA

Definition

The Eye Bank Association of America (EBAA), established in 1961, is a nonprofit organization for the accreditation of eye banks. The EBAA is committed to restoring sight worldwide through the advancement of eye banking, and it has member eye banks in North America, Europe, the Middle East, and Asia. The EBAA strives to raise medical standards for the procurement and distribution of eyes, increase eye donations through advocacy, and ensure that eye bank personnel have received comprehensive training. To date, member banks have restored sight to nearly 1,000,000 individuals.

Cross-References

▶ Cornea
▶ Eye Banking
▶ Keratoconus
▶ Transplantation

Eye Banking

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Definition

Eye banking has evolved over the years from a simple collection and distribution system to a technically demanding and scientifically sophisticated system. In the mid-1970s, an eye bank was a refrigerator where whole eyes were stored at 4 °C until they were used in the operating room for corneal transplantation. Since then, corneal preservation techniques have improved the quality of donor tissue and increased the supply of available donor corneas to meet the increasing demand. Advances in corneal transplantation techniques have led to an increase in corneal transplants and expansion of the indications for transplantation. Patients who were previously considered to be poor prognostic candidates for corneal transplantation are now considered acceptable candidates (Doughman 1998). Today, eye banks provide ocular tissues, including glycerol-preserved corneas and scleral tissue, for multiple procedures, including penetrating keratoplasty, Descemet's stripping endothelial keratoplasty (DSEK), and femtosecond laser-enabled keratoplasty (Heck and Montoya 2011).

The first eye bank was formally established in New York in 1944. Over time, a body of medical standards and regulations has evolved to keep up to date with advancements in eye banking. The goal of these regulations is to insure the highest standard of eye tissue for human transplantation,

while maintaining an adequate donor pool. The Eye Bank Association of America (EBAA) developed the first medical standards of eye banking, which were formally adopted in 1980 (Glasser 2011).

Eye banking involves educating potential donors before death, counseling their next of kin at the time of death, harvesting and preserving the tissue, and finally distributing the tissue to the recipient's surgeon. An eye bank is a complex network of technicians, surgeons, enucleators, medical examiners, and administrators. The process of eye banking is essential to prevent the spread of infectious disease and malignancy from donor to recipient. If microorganisms are transplanted from the donor eye, endophthalmitis may develop and could ultimately result in loss of the eye. Recipient deaths have been reported in cases of rabies virus and Creutzfeldt-Jacob disease transmission. The threat of human immunodeficiency virus (HIV) transmission from donor corneas of patients with acquired immunodeficiency syndrome (AIDS) has been a major concern given the isolation of HIV from the tears, conjunctival epithelium, and cornea of these individuals (Doughman 1998). Additionally, the optical and mechanical integrity of the of the transplanted tissue may be compromised in donors with corneal dystrophies or degenerations, and eye banks are involved in detecting these and other similar abnormalities prior to distribution of tissue to transplant recipients (Glasser 2011).

Cross-References

- ▶ Corneal Dystrophies
- ▶ Femtosecond Laser

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Eye Patch

▶ Corneal Patching

Eyelash Pediculosis

▶ Ocular Lice

Eyelid Crease Incision

▶ Transcutaneous Routes

Eyelid Erythema

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Definition

Eyelid erythema is redness of the eyelids that can result from any condition that irritates, inflames, or infects the eyelid.

Etiology

The delicate, thin skin around the eyes has a rich blood and nerve supply and is susceptible to developing erythema due to many different conditions. The most common causes of eyelid erythema include allergies, inflammation, infection, and trauma.

Classification/Occurrence

Allergies, a very common cause of red eyelids, may be local such as a reaction to a chemical or more generalized such as hay fever. Contact dermatitis occurs frequently from cosmetics, shampoos, soaps, or substances on the hand and fingers that are rubbed inadvertently onto the periocular skin. Notably, preservatives in ophthalmic medications such as benzalkonium chloride and thiomerosal are also potential causes of contact dermatitis.

Other dermatoses may cause eyelid erythema with associated scaling such as seborrheic dermatitis, psoriasis, and atopic dermatitis. Systemic diseases such as cutaneous sarcoidosis can also present with erythematous, scaly plaques, and discoid lupus erythematosus has classically shiny erythematous plaques with punctate, follicular scale that may be seen in the periocular region.

Infections or inflammations of the eyelid margin are also frequent causes of eyelid erythema. These conditions include blepharitis, chalazion, and hordeolum. Other infectious causes may include herpes zoster with its associated painful vesicles in a dermatomal pattern.

Trauma to the periocular region including burns, blunt, or penetrating injury may also lead to eyelid erythema associated with other signs of injury.

Cross-References

► Edema, Eyelid

Further Reading

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Eyelid Inflammation

► Blepharoconjunctivitis

Eyelid Reconstruction

► Reconstructive Surgery of Eyelid

Eyelid Repair

► Reconstructive Surgery of Eyelid

Eyelid Spacer Graft

► Hard Palate Graft

Eyelid Trauma

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Synonyms

Avulsion; Contusion; Hematoma; Lacerations

Definition

Trauma to the eyelid involving damage to the eyelid skin, muscles, connective tissue, mucous membrane, or adnexal structures (Nerad 2001).

Etiology

Eyelid trauma is caused by blunt or penetrating injury. Blunt trauma may result from causes such

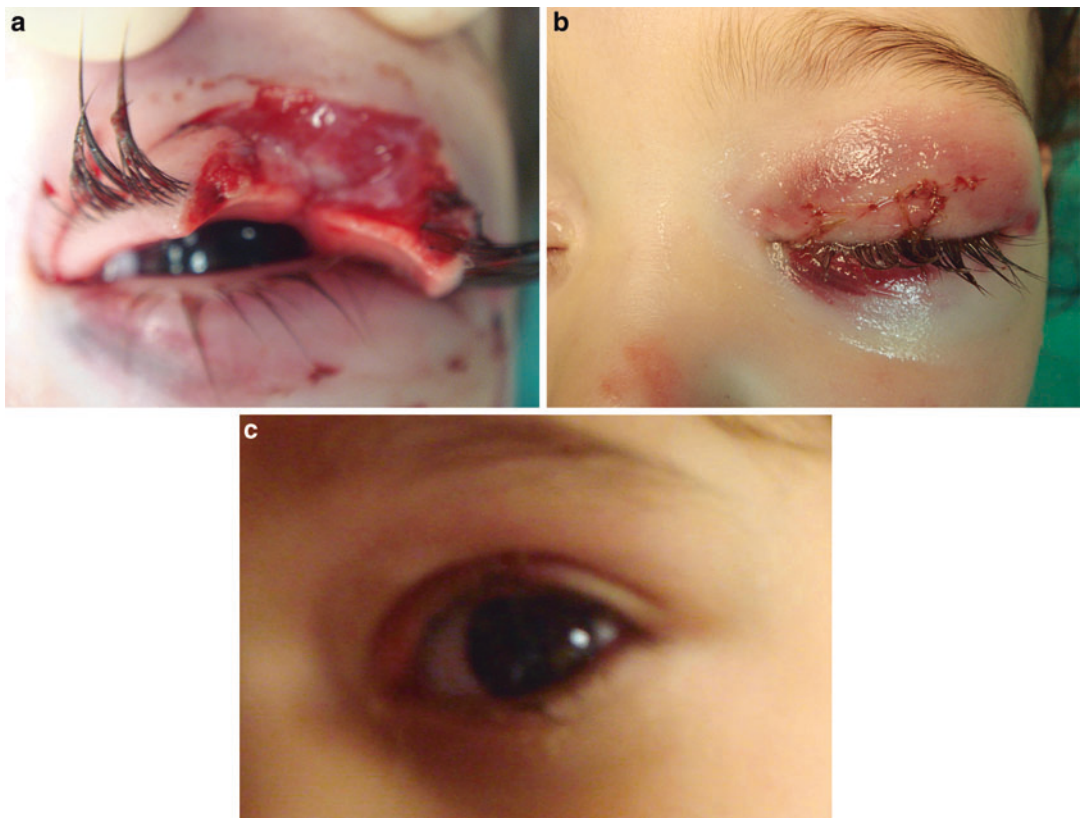
as a motor vehicle accident, assault, or a fall. Laceration or penetrating trauma to the eyelid is seen in the context of assault with sharp object, as well as bite injuries.

Clinical Presentation

Injury to the eyelid or periocular area can be an isolated incident but most often occurs in the setting of multisystem trauma. The physician's primary role is to rule out life-threatening injury and stabilize the patient. Sight-threatening injuries should then be addressed. The eyelid wound is explored to identify injured anatomic structures and the extent of damage. Fat present in the wound implies violation of the orbital septum and consequently, damage to the levator palpebrae superioris muscle is suspected. Full thickness eyelid trauma increases initial suspicion of globe injury. Tissue loss in the context of eyelid trauma is extremely rare but becomes more common with injuries in which the patient has been dragged, such as motorcycle accidents. Shrinkage of tissue is more common. Avulsion of the medial or lateral canthal tendons most often occurs in the setting of blunt trauma. The anterior and posterior arms of the lower eyelid medial canthal tendon are particularly susceptible. With any injury to the medial aspect of the upper or lower eyelid, the ophthalmic examination should inspect for canalicular involvement (Fig. 1a) (Weiner and Bedrossian 2002).

Diagnostics

Examination of the patient's eye precedes examination of the eyelid. Following the eye exam, a



Eyelid Trauma, Fig. 1 (**a**) Initial injury. Eyelid trauma was caused by a fall against a stroller. (**b**) Immediate postoperative result. (**c**) Two week postoperative result.

thorough clinical examination via direct inspection of the wound is the physician's most important tool to determine the location, extent, and severity of the injury. A suspicion of a foreign body in the wound warrants imaging of the region. CT scanning of the orbit is the first line imaging protocol. If the medial aspect of the eyelid is involved, the canalicular system is inspected by careful probing. Damage to the levator is suspected when orbital fat is present within the wound and can be evaluated by measuring the levator excursion of the upper eyelid.

Differential Diagnosis

Trauma to the orbit, periocular trauma.

Prophylaxis

Injury to the eyelid can be prevented by the use of protective eyewear and polycarbonate eye glasses.

Therapy

The goal of treatment is to return normal function and cosmesis to the eyelid. Trauma to the eyelid should be repaired within 48–72 h following injury. The well-vascularized eyelid allows for somewhat delayed closure as it is at lower risk for infection. Some clinicians utilize broad spectrum oral antibiotics until wound treatment is initiated. A general medical history should include inquiry regarding recent tetanus injections. Repair of the wound involves reapproximating tissues to their appropriate anatomic locations. If the levator muscle is found to be damaged, it is sutured to the anterior border of the tarsus. Furthermore, if canalicular trauma is involved, the canalicular system should be explored, repaired, and intubated with silicone tubes. Medial or lateral canthal tendon avulsions are repaired by reinserting the appropriate limb of the canthal tendon to its bony insertion (Fig. 1b, c).

Prognosis

Given the highly vascular nature of the eyelid, wounds heal with minimal scarring and eyelid asymmetry.

Epidemiology

Eyelid injury predominantly occurs in males aged 20–30 (Savar et al. 2008).

Cross-References

- ▶ Open Globe
- ▶ Orbital Floor Fracture
- ▶ Orbital Pain
- ▶ Penetrating Eyelid Injuries
- ▶ Trauma, Canalicular
- ▶ Trauma, Lacrimal Sac and Nasolacrimal Duct

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Eyelid Weights

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Synonyms

Upper lid loading

Definition

Eyelid weight insertion is a lid loading technique using an implanted device to counter lagophthalmos associated with facial paralysis.

Indication

Facial paralysis places the eye at risk for incomplete closure voluntarily and during blinking due to paralysis of the orbicularis oculi and the unopposed action of the levator palpebrae superioris. Inadequate corneal protection results in exposure keratitis and corneal ulceration and, in severe cases, may result in blindness. In addition, chronic facial paralysis may result in ectropion of the lower lid, brow ptosis, and decreased tear production, further contributing to corneal injury. Co-existing corneal anesthesia, dry eye, and absent Bell's phenomenon put patients at greater risk of ocular complications. The most common causes of facial paralysis include Bell's palsy, tumors such as acoustic neuroma, trauma to the seventh cranial nerve, cerebral vascular accidents, and complications of previous facial or neurosurgical surgery.

Various implanted devices have been tried to counteract the action of the levator including silicone bands, palpebral springs, and lid magnets. However, due to complications of breakage, erosion, and extrusion, their use is currently limited.

Upper lid loading with gold weight insertion is now the most commonly performed procedure for the treatment of paralytic lagophthalmos due to its safety, predictability, and low cost. It was first described in 1958 by Illig and further refined in its design and surgical technique over the past several decades. Weighting of the upper lid results in increased gravitational pull on the lid and with relaxation of the levator on attempted eye closure, the eyelid passively closes by gravitational effect. Gold has the advantage of combining considerable density with malleability, being relatively inert and providing a good color match for the skin. In addition, gold weight insertion is associated with the fewest number of complications and is reversible.

Contraindication

Eyelid weight procedures are indicted for long-standing cases of facial paralysis or when the chance of recovery is low. If early spontaneous recovery of the nerve function is predicted, aggressive lubrication with temporary tarsorrhaphy should be considered. The procedure is also contraindicated in cases of gold allergy.

Techniques and Principles

The appropriate gold weight size is selected preoperatively by taping various sizes of weights to the upper eyelid to determine which size best achieves adequate relaxed eyelid closure while limiting eyelid ptosis in primary gaze. Once the appropriate weight is determined, a customized weight is made for the patient, taking into account the overall size of the lid and the curvature of the globe.

A standard upper eyelid incision closure is made through skin and orbicularis muscle. The gold weight is then positioned in a pocket overlying the tarsal plate. The implant is then sutured to the tarsal plate in order to reduce the risk of migration and extrusion.

Outcome

Gold weight implantation does not restore the normal blink reflex but reduces lagophthalmos and corneal exposure by improving voluntary eye closure.

Complications

Complications of gold eyelid weights include undercorrection, overcorrection (ptosis), allergy or foreign body reaction, cosmetic deformity, corneal astigmatism, infection, migration, and extrusion.

Cross-References

- ▶ Bell's Palsy
- ▶ Lagophthalmos

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Eyelid Weights, for Exposure Keratopathy

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Synonyms

Upper lid loading

Definition

Eyelid weights are metal weights implanted into the upper eyelid to provide additional weight. This is done to prevent keratopathy resulting from lagophthalmos.

Cross-References

- ▶ Eyelid Weights
- ▶ Lagophthalmos

F

Facial Diplegia, Guillain-Barré Syndrome

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Definition

Facial diplegia refers to facial nerve paralysis of both sides of the face. It can be a finding in patients with Guillain-Barre Syndrome (GBS), an infection-triggered polyneuropathy disorder affecting the peripheral nervous system.

Differential Diagnosis

Other diseases that can present with facial diplegia include Bell's palsy (which is usually unilateral), chronic inflammatory demyelinating polyneuropathy (CIDP), sarcoidosis, severe vitamin B1 deficiency, acute arsenic poisoning, n-hexane (glue-sniffing) neuropathy, vasculitis, Lyme disease, porphyria, tick paralysis, leptomeningeal disease, and paraneoplastic disease.

Diagnosis

The diagnosis of GBS is based on clinical presentation. Key features that favor a diagnosis of GBS include relative symmetry of ascending polyneuropathy (e.g., muscle weakness and sensory impairment), cranial nerve involvement (including Miller Fisher variant), areflexia, autonomic dysfunction, normal body temperature, and elevated CSF protein levels with normal cell count (albuminocytologic dissociation).

Pathogenesis

The pathogenesis of GBS is believed to be autoimmune. Following an infection, antibodies generated in the immune response cross-react with components of peripheral nerves, particularly

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myelin-producing Schwann cells. This phenomenon is known as molecular mimicry, and the result is secondary demyelination and dysfunction of peripheral nerves. *Campylobacter jejuni*, which often causes a diarrheal illness, is a common precipitating infection in GBS. Other infectious etiologies include viruses, other bacteria, and some immunizations.

Clinical

GBS usually progresses over a period of about 2 weeks. GBS that progresses longer than 8 weeks is more consistent with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).

Treatment

Supportive care is of utmost importance in individuals suffering from GBS, particularly for respiratory failure. Severe autonomic dysfunction often requires close monitoring in an ICU setting, with particular attention given to blood pressure control, arrhythmias, ileus, urinary retention, and other autonomic functions. Neuropathic pain is common and can be treated with medications like gabapentin or carbamazepine.

Plasma exchange can be done to remove the presumptive autoimmune antibodies from the blood, and intravenous immune globulin (IVIG) can be administered to inhibit production of more autoimmune antibodies by B cells. Both of these therapies can help increase recovery time.

Prognosis

The prognosis varies by severity of illness. Poor prognostic factors include older age, rapid onset (less than 7 days), severe muscle weakness, need for ventilator support, and a preceding diarrheal illness.

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Facial Nerve

► Cranial Nerve VII

Facial Nerve Palsy

► Seventh Nerve Palsy

Facio-Auriculo-Vertebral Spectrum

► Goldenhar Syndrome

Familial Adenomatous Polyposis

► Gardner Syndrome: Retinal Pigment Epithelium Hypertrophy

Familial Alpha-Lipoprotein Deficiency

▶ Tangier Disease, Corneal Changes

Familial Amyloidosis, Finnish Type

▶ Meretoja Syndrome

Familial Cerebello-Retinal Angiomatosis

▶ Hemangioblastomas, with Retinal Angiomatosis (von Hippel Lindau Disease)
▶ Retinae (Retinal Angiomatosis, von Hippel Syndrome/Disease)
▶ VHL Syndrome

Farsighted Shift

▶ Hyperopic Shift

Farsightedness

▶ Hyperopia

Fascia Bulbi

▶ Tenon's Capsule

Femtosecond Laser

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F

Synonyms

Ultrashort pulse laser, Ultrafast laser

Definition

A femtosecond (fs) laser is a laser which emits optical ▶ pulses with *ultrashort pulses*, between a few and hundreds of fs (1 fs $= 10^{-15}$ s).

Epidemiology

Today, almost a dozen of different companies offer fs laser devices for ophthalmic surgical use. Fs laser technology has now been used in an estimated number of five million plus surgical procedures worldwide.

History

The first studies regarding fs laser technology were published in the 1980s investigating the interaction of the fs laser with retinal tissue in the animal model. The human cornea was treated for the first time in 1994 (Kautek et al. 1994). Since 2001, different fs laser systems were introduced on the market, and fs laser technology was

basically used as an alternate for the mechanical microkeratome in laser in situ keratomileusis (Kohnen et al. 2010).

Clinical Features

The fs laser works with a wavelength of 1030–1050 nm as this wavelength is suitable for corneal procedures due to very low light absorption or dispersion. The laser achieves its surgical effect through a process termed "photodisruption." When the intensity of the focused laser beam exceeds the threshold of 10^{10}–10^{11} W/cm^2, changes occur in the absorption characteristics of the tissue, and the phenomena of "laser-induced optical breakdown" occur. A plasma of free electrons and ions is generated. When energy is removed from the system, these electrons and ions recombine to form a gas (cavitation bubble) that expands rapidly within the tissue. Expanding of the gas produces a cleavage of the tissue surrounding the focal point of the laser. If these laser spots are placed close together side to side, lamellar cuts can be generated; if the spots are stacked on top of each other, vertical cuts can be generated.

Tests

Before each clinical application, this type of laser usually performs a self-test.

Differential Diagnosis

Other important laser systems used for ophthalmic surgical procedures are, e.g., the excimer laser, the Nd:YAG (neodymium-doped yttrium aluminum garnet) laser, the argon laser, the diode laser, or the carbon dioxide laser.

Etiology

The term "femto" originates from Danish "femten" which means "fifteen." One femtosecond is 10^{-15} s.

The word "LASER" is short for light amplification by stimulated emission of radiation.

Treatment

Fs laser technology is implemented in corneal refractive surgery and recently also in cataract surgery. Common applications are used as a laser keratome for laser in situ keratomileusis, for lamellar or penetrating keratoplasty (especially for differentiated cut configurations like the "top-hat" or "mushroom" configuration), for creating intrastromal tunnels for intracorneal ring segment implantation, for astigmatic keratotomy, or for femtosecond lenticule extraction (where extraction of a fs laser-generated lenticule replaces excimer laser photoablation) (Kook et al. 2009). Recent research also implicates fs laser technology for capsulorhexis and fs laser-assisted phacofragmentation.

Cross-References

► Astigmatic Keratotomy

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Femtosecond Laser-Assisted Lamellar Keratoplasty

► Anterior Lamellar Keratoplasty, Laser Assisted

Ferry Line

▶ Iron, Corneal Deposits of

Fibroma

▶ Neurofibromas, Discrete

Fibrous Papule

▶ Angiofibromas, Facial, in Tuberous Sclerosis

Fibrovascular Pannus

▶ Pannus/Micropannus

15 mg Anecortave Acetate Depot Suspension

▶ Anecortave Acetate (RETAANE), for Age-Related Macular Degeneration

Fine Needle Aspiration (FNA)

▶ Fine-Needle Aspiration Biopsy (FNAB) of Orbit

Fine-Needle Aspiration Biopsy (FNAB) of Orbit

Yasaman Mohadjer
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Synonyms

Fine needle aspiration (FNA)

Definition

A procedure used to remove a small amount of an unknown lesion by aspirating through a syringe. This allows a small tissue sample, often in patients with known lymphoproliferative disease, metastatic disease, or secondary tumors from adjacent sinus spread.

Indications

To safely obtain a tissue sample without a surgical orbitotomy. This technique may be reserved for patients with blind eyes, who may be poor surgical candidates or when immediate biopsy result is required.

Contraindication

Relative contraindication for tumors that may be near vital structures (i.e., optic nerve) or patients unable to tolerate procedure. FNA is also contraindicated for tumors that may metastasize if violated (some lacrimal gland tumors, melanomas, etc.) and should be avoided (Tijl and Koornneef 1991).

Techniques and Principles

This procedure may be done in the office. The patient is given an injection of local anesthetic. Then, a 4-cm 22 gauge needle is passed transcutaneously or transconjunctively to the suspicious lesion and cells are aspirated. Occasionally, it is performed via computed tomography (CT) or ultrasound guidance for improved localization (Tijl and Koornneef 1991).

Outcome

A small sample size is obtained while avoiding surgery.

Complications

The sample size may be insufficient, and further FNA or surgery may be required. Pain, infection, swelling, and bruising may occur. Rarely there may be hemorrhage or hematoma. A retrobulbar bleed, while possible, is a rare complication.

Cross-References

▶ Lymphoma: Definition
▶ Orbit, Inflammation of

References

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First and Second Branchial Arch Syndrome

▶ Goldenhar Syndrome

Fisher's One-and-a-Half Syndrome

▶ One-and-a-Half Syndrome

Fisher's Syndrome

▶ Miller Fisher

Fisherman's Keratopathy

▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
▶ Keratinoid (Spheroidal) Degeneration
▶ Spheroidal Degeneration

Flash Burn

▶ Arc Welding, Occupational Light Injury and

Fleck Dystrophy

▶ Corneal Dystrophies

Fleischer Ring

▶ Iron, Corneal Deposits of

Flomax™

▶ Tamsulosin

Floor Fracture

▶ Blowout Fractures

Floury Cornea

▶ Cornea Farinata

Fluorescein Breakup Time (FBUT)

▶ Tear Breakup Time

Fluorescein, as Diagnostic Agent

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Definition

Fluorescein angiography (FA) is a diagnostic modality that utilizes intravenous sodium fluorescein to image retinal and choroidal blood vessels (Gass 1997; Johnson et al. 2006).

Purpose

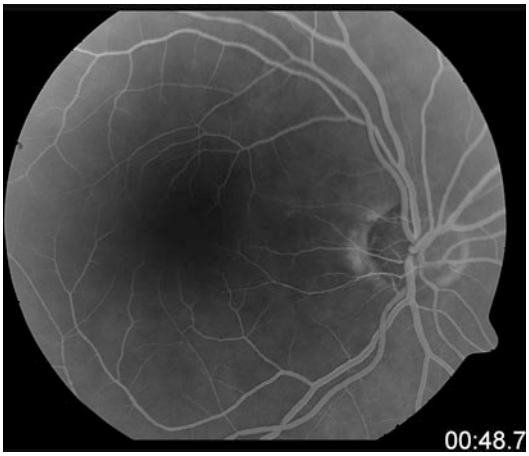
Fluorescein angiography provides photographic documentation on the location and condition of retinal and choroidal blood vessels, allowing clinicians to diagnose and treat retinal and choroidal diseases.

Principle

Fluorescein angiography is based on the ability of sodium fluorescein to absorb photons of light in the blue wavelength (465–490 nm) of light and subsequently emit them in the yellow-green wavelength (520–530 nm) of light. Following intravenous injection, sodium fluorescein shortly appears within the eye and outlines the location of retinal and choroidal blood vessels. The documentation of this fundus appearance is accomplished with a special FA camera, which harbors a blue wavelength outbound filter over its light source and a yellow wavelength inbound filter over its objective lens. Fluorescein angiography images appear in black and white (Fig. 1).

The specific technique of FA involves intravenously injecting sodium fluorescein through a peripheral site (usually the antecubital vein) followed immediately by photographing the fundus oculi with the FA camera. Within 8 to 12 seconds of the injection, sodium fluorescein appears within the choroidal vasculature followed almost immediately within the retinal arteries (arterial phase). Over the next 30 s, sodium fluorescein traverses the retinal capillaries and flows via a laminar fashion into the retinal veins (laminar venous phase). Eventually, both retinal arteries and veins are completely filled (arteriovenous phase). The angiogram finishes over the next 15 min as sodium fluorescein recirculates throughout the body and the fluorescent images in the fundus fade.

Pathologic findings on FA reflect an abnormal ability of sodium fluorescein to accumulate in areas of the eye where it should not be, or inability to be present in areas where it should, such as retinal and choroidal vessels. These abnormalities are referred to as hyperfluorescence and hypofluorescence, respectively. (Autofluorescence is the ability of a fundus object to fluoresce even without any injection of sodium fluorescein.)



Fluorescein, as Diagnostic Agent, Fig. 1 Fluorescein angiography of the ocular fundus

During a normal FA, sodium fluorescein cannot pass through the retinal pigment epithelium or tight junctions of the retinal vessels and so cannot enter the subretinal, intraretinal, or vitreous spaces. However, pathologic conditions often alter these natural barriers, and sodium fluorescein appears to leaks into abnormal locations. The increased presence of sodium fluorescein produces a signal brighter than expected (hyperfluorescence). When sodium fluorescein cannot fill a vascular structure like it normally should (i.e., an occluded retinal or choroidal vessel), the decreased amount of sodium fluorescein produces a signal darker than expected (hypofluorescence). Hyperfluorescence and hypofluorescence can also be observed when less or more of an obscuring substance is present over a normal pattern of fluorescence and produces a brighter or darker image, respectively. Common intraocular substances that influence the brightness of fluorescence in such a manner include blood, pigment, lipid, and fibrosis.

Indications

Common indications for FA include diabetic macular edema, age-related macular degeneration,

branch and central retinal artery or vein occlusions, proliferative diabetic retinopathy, infectious and inflammatory retinochoroidal diseases, and posterior segment neoplasms. However, FA may be helpful and considered for any ocular disease that involves the vascular supply of the retina and choroid or that affects the integrity of the blood-retinal barrier.

Contraindications

Fluorescein angiography is contraindicated in patients who have had a prior severe reaction to fluorescein, including urticaria and anaphylaxis. It should also be used with caution in patients with hepatic or renal compromise as they may display decreased clearance of the drug. Patients with a protein-deficient state can experience an effectively higher level of free fluorescein due to decreased serum protein and may require a reduction in dosage of fluorescein.

Advantages/Disadvantages

Advantages of FA are many since it is safe, well tolerated, and easily performed in a clinic setting and provides valuable information in the diagnosis and treatment of many retinal and choroidal diseases. Potential disadvantages of FA include its limited ability to image the choroidal circulation and its potential side effect profile, including the ability to induce nausea, vasovagal reactions, urticaria, and anaphylaxis.

Cross-References

- ▶ Angiography, Fluorescein
- ▶ Central Retinal Artery Occlusion, Ocular Ischemic Syndrome
- ▶ Neovascular Glaucoma in Ischemic Central Retinal Vein Occlusion
- ▶ Retinal Blood Vessels
- ▶ Retina, Structure of

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Flutex

- ▶ Intravitreal Triamcinolone

Flutter, Ocular

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Synonyms

Saccadic nystagmus

Definition

Ocular flutter is defined as involuntary, back-to-back, rapid, horizontal saccades without an intersaccadic interval.

Etiology

Ocular flutter is commonly associated with cerebellar or brainstem disease but can occur in the setting of postviral encephalopathy. One hypothesis is that ocular flutter is a disorder of the saccadic pause neurons, but this has not been proven.

Clinical Presentation

Patients may present with symptoms of benign encephalitis – ataxia and rapid ocular movement while the eyes are closed.

Diagnostics

Neuroimaging of the posterior fossa is typically the first-line evaluation of ocular flutter. Lumbar puncture may be required in some cases (e.g., postinfectious). Some cases are paraneoplastic in origin, and a search for underlying neoplasm may be indicated.

Differential Diagnosis

Opsoclonus, nystagmus

Therapy

Treatment is dependent upon the underlying disease.

Prognosis

Prognosis depends on the etiology of the flutter.

Epidemiology

Ocular flutter is typically postinfectious or paraneoplastic but can affect any age, either gender, and any ethnic group.

Cross-References

▶ Nystagmus: Overview

Further Reading

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Focal Dystonia

▶ Benign Essential Blepharospasm: Neuro-ophthalmic Considerations

Focal Grid Laser

▶ Early Treatment Diabetic Retinopathy Study (ETDRS)

Focal Laser

▶ Early Treatment Diabetic Retinopathy Study (ETDRS)

Focimeter

▶ Lensmeter

Focusing Spasm

▶ Accommodation, Functional (Nonorganic/Nonphysiologic) Disorders of

Foldable Intraocular Lens

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Synonyms

Foldable IOL

Definition

A foldable intraocular lens is literally folded to half its size. It makes an insertion of the IOL into the eye through a small incision possible. Incision may be as small as 1.8 mm. Once a foldable IOL is placed, it unfolds to its full regular size.

Epidemiology

Today the vast majority of worldwide implanted IOLs are foldable IOLs. PMMA IOLs are used only in special cases.

History

The first foldable IOLs were developed in the 1950s. They were made of hydrogel and implanted in animals by M. Dreifus. Later in the 1970s, E. Epstein implanted these IOLs in human eyes. The first foldable silicone IOL was used in 1978 by J. Zhou. In the 1980s, foldable IOLs conquered the market. Until that time, PMMA IOLs were the standard IOLs requiring a 5–7 mm incision after extracapsular surgery (Werner 2008; Auffahrt 2008). As implantation was often performed in the ciliary sulcus, a so-called windshield-wiper effect was noticed. This referred to a pigment dispersion of the posterior pigment epithelium of the iris due to mobility of the IOL. This type of post-operative complication became rare as foldable IOLs were implanted with injector systems into the capsular bag in the 1990s. Today, also phakic IOLs like the iris-supported Artiflex/Veriflex IOL or anterior chamber angle-supported AcrySof are implanted with injector systems.

Clinical Features

A foldable IOL is made of silicone or hydrophobic or hydrophilic acrylic. Foldable IOLs have numerous advantages over rigid PMMA IOLs (Kohnen et al. 2009):

- The IOL can be implanted or injected via a small incision and is therefore less traumatic.
- Placement of the IOL is easier and more accurate.
- Low risk of tilting of the IOL.
- Faster wound healing due to small incision size.
- Less surgical induced astigmatism due to small incision size.

Tests

In the scope of a biomicroscopic examination, it is not possible to determine whether a foldable or non-foldable IOL is implanted in the eye.

Differential Diagnosis

Either aphakic, pseudophakic, or phakic IOL is manufactured as foldable models.

Etiology

Today, all different types of IOLs – monofocal, multifocal, accommodative, toric, and blue light filter – are available on the market.

Treatment

See entries "► Cataract Surgery" and "► Intraocular Lens."

Cross-References

► Acrylic IOL
► Cataract Surgery
► Intraocular Lens
► Refractive Lens Exchange

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Foldable IOL

► Foldable Intraocular Lens

Follicular Conjunctivitis

► Adenoviral Keratoconjunctivitis

Follicular Keratosis

► Papillomas, Eyelid

Fong Disease

► Onychoosteodysplasia (Nail-Patella Syndrome)

Forced Duction Test

► Duction Test

Fornices

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Definition

Loose arches of redundant conjunctival tissue posterior to the upper and lower eyelids.

F

Structure

The conjunctiva of the fornices joins the palpebral (tarsal) and bulbar segments and consists of non-keratinized cuboidal epithelial cells with prominent microvillae. It overlies a substantia propria rich in lympthoid tissue and accessory lacrimal glands (glands of Krause) (Song et al. 2006).

The apex of the superior fornix is located approximately 10–13 mm above the superior lid margin when the eyes are open and 25 mm above the margin when they are closed (Bedrossian 2006). It is suspended by ligaments originating from the levator/superior rectus complex. The lacrimal gland ductules drain into the superolateral fornix. The deepest extent of the inferior fornix is 9–10 mm below the inferior lid margin. It is maintained by ligaments originating from the inferior rectus sheath. The lateral fornix extends to the globe equator. The plica semilunaris and caruncle take the place of the fornices medially.

Function

The redundant tissue of the conjunctival fornices permits unimpeded movement of the globe in all directions. The highest concentration of mucin-producing goblet cells is contained within the fornices. The glands of Krause (along with the glands of Wolfring along the antimarginal border of the tarsal plates) are responible for the basal secretion of aquous tears. The fornices therefore play a critical role in ocular surface health.

Clinical Relevance

Forshorneting of the fornices and symblepharon may occur with autoimmune disorders such as Stevens-Johnson syndrome (SJS) and ocular-cicatricial pemphigoid (OCP), chemical burns, surgical trauma, trachoma, and other forms of cicatrizing conjunctitivits. In severe cases, prompt intervention is required to prevent diplopia, lid malposition, xerosis, and corneal blindness.

Deep fornices are required after enucleation and evisceration in order to support an adequately sized prosthesis. Fornix contraction is often treated with mucus or amiotic membrane grafts (Solomon et al. 2003; Demirci et al. 2010).

Giant fornix syndrome is typically seen in older individuals with chronic ocular surface inflammation (Rose 2004). Profound redundancy of the fornices contributes to the trapping of mucoid material and colonization with *Staphylococcus aureus*. This results in chronic or recurrent ocular discharge and conjunctivitis that is refractory to conventional treatements. Difinitive treatment is with resection of the excess conjunctiva.

Cross-References

- ▶ Conjunctiva
- ▶ Goblet Cells, Mucin Tear Secretion by
- ▶ Palpebral Conjunctiva
- ▶ Stevens Johnson Syndrome
- ▶ Symblepharon

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4′-Dione Retinopathy

▶ Canthaxanthin, Retinopathy

Fourth Cranial Nerve Palsy

▶ Fourth Nerve Palsy

Fourth Nerve Palsy

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Synonyms

Fourth cranial nerve palsy; Trochlear nerve palsy

Definition

The fourth cranial nerve, or trochlear nerve, innervates the superior oblique ocular muscle. Its nucleus lies in the midbrain caudal to the oculomotor nucleus, dorsal to the medial longitudinal fasciculus, and at the level of the inferior colliculus (Lee and Brazis 2003). The fourth nerve travels inferior and posteriorly, exits dorsally, and decussates at the anterior medullary velum, passing between the posterior cerebral artery and the superior cerebellar artery in the subarachnoid, before entering the orbit through the superior orbital fissure and innervating the superior oblique muscle. Any lesion along this pathway can result in a fourth nerve palsy (FNP). An FNP manifests as an ipsilateral hypertropia in primary position, worse in contralateral gaze, and ipsilateral head tilt. There is also often objective and subjective ipsilateral excyclotorsion. As with all ocular motor cranial neuropathies, there are a wide range of known etiologies (i.e., neoplasms, infections, metabolic disorders, and ischemia), but the most common causes of isolated fourth nerve palsies are traumatic, congenital, and microvascular etiologies (Lee and Brazis 2003; Brazis 2009). The distinction between isolated and non-isolated FNP (i.e., other neurological signs and symptoms are present) is important since cases of isolated FNP often do not need further neurological workup or neuroimaging.

Etiology

In most series of FNP, the most common cause is head trauma accounting for up to 40% of all cases (Keane 1993; Mollan et al. 2009; Von Noorden et al. 1986). The fourth cranial nerve is the longest and thinnest of all the cranial nerves and is thus most susceptible to shearing injury at the free margin of the tentorium cerebella and can be damaged even in cases of relatively mild head trauma. In cases of traumatic FNP, the diplopia will typically have a clear temporal relationship to the previous head trauma, does not progress, and is often neurologically isolated. Trauma is also a common cause of bilateral FNP, and in these cases, there might not be as large of a primary position hypertropia (HT) as in a unilateral FNP. Instead there might be a reversing HT in right and left gaze or alternating HT in alternating head tilts and a larger than expected ($>10^{\circ}$) amount of excyclotorsion (Brazis 2009).

Congenital FNP is another common etiology (Lee and Brazis 2003; Brazis 2009) and may be subtle in childhood and worsen in adulthood due to decompensation (thought to be a breakdown of vertical fusion rather than progressive superior oblique dysfunction). These types of patients often complain of neck pain from chronic head tilting and may have facial asymmetry or sternocleidomastoid hypertrophy. Old photographs of the patient showing a long-standing head tilt will often help in establishing this diagnosis, and large vertical fusional amplitudes (greater than 6–8 prism diopters) in primary gaze are more suggestive of congenital cases. The excyclotorsion is often asymptomatic in congenital FNP cases but symptomatic in acquired cases.

Microvascular ischemia can cause isolated FNP including diabetes mellitus and hypertension (Lee and Brazis 2003). Most vasculopathic FNPs resolve in 3–6 months, and progression or lack of resolution should prompt consideration for neuroimaging and other evaluations. Other less common causes of isolated FNP include midbrain lacunar infarction, increased intracranial pressure (e.g., pseudotumor cerebri, subarachnoid hemorrhage), and posterior fossa tumors – however, these etiologies are typically associated with other neurological and clinical findings.

Clinical Presentation

The principle presenting symptom in patients with unilateral FNP is binocular vertical diplopia that is often accompanied by a compensatory contralateral head tilt (Lee and Brazis 2003; Brazis 2009). The head tilt minimizes the vertical diplopia by moving the eye away from the paretic superior oblique muscle's field of action. Rarely, however, some patients with an FNP may adopt an ipsilateral head tilt to increase rather than decrease the

vertical deviation, which produces a greater distance between the two images and an increased ability for some patients to ignore the second image. The superior oblique muscle (SOM), which is innervated by the fourth cranial nerve, has three functions that are dependent on the position of gaze: (1) primary function in primary position, incyclotorsion (or intorsion) of the eye; (2) secondary function, depression (or infraduction) of the globe when the eye is in the adducted position; and (3) tertiary function, abduction of the eye (Lee and Brazis 2003; Brazis 2009). The direct antagonist of the superior oblique muscle is the ipsilateral inferior oblique muscle. With a fourth nerve palsy, there may be **underaction** of the ipsilateral superior oblique muscle and thus apparent **overaction** of the ipsilateral inferior oblique muscle, which acts (among other functions) to elevate the eye. Therefore, a hypertropia will be observed in the affected eye which is greater in contralateral gaze (due to overaction of the ipsilateral inferior oblique in adduction) and head tilt toward the affected eye.

Excyclotorsion of the affected eye, due to weakness of the incyclotorsion action of the superior oblique, is another potential symptom of FNP. It can be observed objectively on fundus exam or can be measured subjectively using a double Maddox rod. Anatomically, the fovea is usually about one-third of a disk diameter below the center of the optic disk. If the fovea is lower than expected, excyclotorsion is present. In the double Maddox rod test, a Maddox rod is placed in front of each eye in a trial frame with the grooves oriented vertically (producing parallel horizontal lines when the patient looks at a light source). If the lines are not parallel, cyclotorsion is present and the patient is asked to adjust the rods until the lines are oriented parallel on the horizontal axis. If excyclotorsion is present, the patient will turn the OD Maddox rod counterclockwise or the OS Maddox rod clockwise.

Bilateral FNP, accounting for 10–30% of all cases, is usually the result of trauma but can also be caused by increased intracranial pressure, Chiari I, tumor, or other intracranial pathologies (Keane 1993; Mollan et al. 2009; Von Noorden et al. 1986). In primary gaze, there is often minimal ocular misalignment due to the bilateral nature of involved muscles (a bilateral HT cancels out). Due to decreased superior oblique muscle abduction, an esotropia may be present in either eye that is worse on downgaze, classified as a V-pattern esotropia if there is a 15 prism diopter or greater difference between upgaze and downgaze (Brazis 2009). This often complicates the diagnosis and is often deceptively suggestive of sixth nerve palsy. The hypertropia may also alternate such that it is contralateral to the direction of gaze and ipsilateral to the direction of head tilt. There is often a large angle of excyclotorsion ($>10^{\circ}$) that is accompanied by prominent torsional diplopia. In any patient with excyclotorsion greater than 10°, bilateral superior oblique palsy should be suspected.

Diagnostics

The initial evaluation of any patient presenting with a unilateral vertical misalignment involves using the Parks-Bielschowsky three-step test to determine the paretic muscle (Lee and Brazis 2003). Only eight muscles are involved in vertical ocular alignment: the right superior rectus (RSR), the right inferior rectus (RIR), the right superior oblique (RSO), the right inferior oblique (RIO), the left superior rectus (LSR), the left inferior rectus (LIR), the left superior oblique (LSO), and the left inferior oblique (LIO). Each of the three steps of the Parks-Bielschowsky test is designed to eliminate one or more of the muscles listed above such that after all three steps are performed, only one muscle is isolated as the affected or paretic muscle.

The first step of the test involves determining the side and size of the hypertropia in primary position. For example, if there is a right hypertropia (RHT), the paretic muscle can be either of the right eye depressors (RIR, RSO) or either of the left eye elevators (LSR, LIO). Conversely, in the case of left hypertropia, the paretic muscles can be the LIR or LSO or RSR or RIO.

The second step involves determining whether the hypertropia is worse on right or left gaze. The recti muscles have a greater vertical action when

the eye is in an abducted position, while the oblique muscles have a greater vertical action when the eye is in an adducted position. Thus, for the affected or hypertrophic eye, the paretic muscle should be a vertical rectus muscle if the hypertropia worsens in abduction or an oblique muscle if the hypertropia worsens in adduction. For example, for a right hypertropia, if the RHT worsens on right gaze, the paretic muscle is the RIR or LIO. If the right hypertropia worsens on left gaze, the paretic muscle is either the RSO or LSR.

The third step is to determine whether the hypertropia is worse on right or left head tilt. The superior muscles (SR, SO) intort the eye, while the inferior muscles (IR, IO) extort the eye. In a head tilt, the eye ipsilateral to the direction of the tilt (i.e., right eye in right head tilt or left eye in left head tilt) will intort (through action of the SR and SO), and the contralateral eye will extort (through action of the IO and IR). Thus, the hypertropia, or vertical deviation, will be increased in a head tilt ipsilateral to the affected eye if one of the intorting muscles is paretic (SR or SO). Likewise, the hypertropia will be increased in a head tilt contralateral to the affected eye if one of the extorting muscles is paretic (IR or IO).

Thus, after the conclusion of the three steps, only one muscle should remain as the affected, or paretic, muscle through the process of elimination. An additional "fourth step" can be added to test for the presence of any torsion using the double Maddox rod.

If the superior oblique muscle is determined to be the paretic muscle, the next step involves determining whether the cranial nerve deficit is isolated or non-isolated (Lee and Brazis 2003; Brazis 2009). If the FNP is non-isolated, neuroimaging, preferably magnetic resonance imaging (MRI) of the brain and orbits with and without contrast and fat suppression, is required and should be directed at the anatomical location of neurological pathology. Important etiologies of non-isolated FNP can include intracranial malignancy, intracranial hemorrhage, infarction, demyelinating disease, cavernous sinus thrombosis, orbital apex syndrome, and toxic/nutritional polyneuropathy. In patients with an isolated, acute FNP, it is important to first consider the more common congenital, traumatic, and microvascular etiologies. In cases of isolated presumed vasculopathic FNP, if symptoms and signs do not improve or worsen after months of observation, the initial diagnosis should be questioned and the patient must undergo neuroimaging, preferably MRI as stated above. Computed tomography (CT) scanning should be utilized in cases of suspected bone trauma or hemorrhage. It is also important to re-evaluate for syndromes that can initially mimic a fourth nerve palsy such as myasthenia gravis, giant cell arteritis (in an older patient), skew deviation, and thyroid eye disease.

F

Differential Diagnosis

Several conditions can initially mimic a fourth nerve palsy but often progress to produce other neurological and/or orbital findings (Lee and Brazis 2003; Brazis 2009). Restrictive strabismus can be produced by a variety of orbital processes (e.g., Graves ophthalmopathy, orbital tumors, orbital fracture, orbital pseudotumor) that are often accompanied by orbital signs such as proptosis, chemosis, and conjunctival injection. Myasthenia gravis can mimic any painless ophthalmoplegia and is often accompanied by ptosis and fatigability. Temporal arteritis can also manifest as ophthalmoplegia and is commonly associated with scalp tenderness, temporal nodularity, and/or jaw claudication. Skew deviation, resulting from pathology of the vestibule-ocular pathways, manifests as any type of vertical misalignment and can present with hypotropia, excyclotorsion, and a head tilt. The vertical misalignments are often position dependent in skew deviation and position independent in fourth nerve palsy. A change in vertical misalignment during an upright to supine test is highly sensitive and specific for skew deviation. Skew deviation is also commonly associated with more symptoms and signs of brainstem pathology.

Prophylaxis

Non-applicable

Therapy

Treatment should be directed toward the underlying etiology of the trochlear nerve palsy. In general, isolated FNPs that are traumatic, congenital, or microvascular most often resolve and should be observed several months before further intervention is considered (Lee and Brazis 2003; Brazis 2009). Surgery, usually consisting of inferior oblique weakening (myomectomy with disinsertion, recession, etc.) or less commonly a superior oblique strengthening procedure, is considered only after conservative measures fail, an etiologic diagnosis has been established, and there has been stability of the ocular misalignment for a period of at least 6 months. A trial of base-down prism over the hypertrophic eye is usually attempted prior to surgery; however, this method does not correct torsional diplopia, and many patients find prism correction unsatisfactory if they have a large torsional component. Patching one eye can be beneficial in patients who defer surgery but should be used with caution in children that fall in the amblyopic age range.

Cross-References

- ▶ Fourth Cranial Nerve Palsy
- ▶ Trochlear Nerve Palsy

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Fovea, Foveal Avascular Zone (FAZ)

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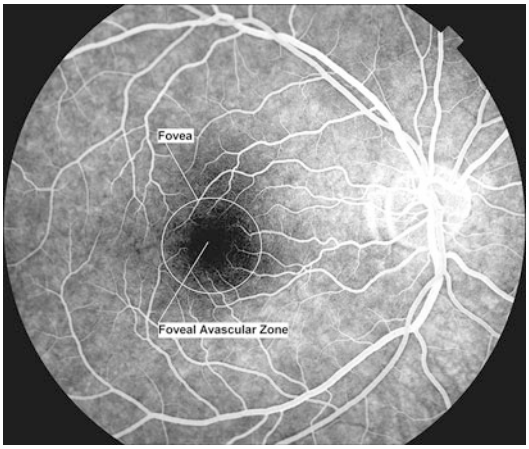
Definition

Anatomical area of retina with highest visual acuity that is responsible for central vision.

Basic Characteristics

The clinical fovea appears as a circular area of the retina (approximately 1.5 mm in diameter) lying approximately 17° (4500–5000 μm) directly temporal to the optic nerve (Gass 1997; Massey 2006). It is responsible for central and color vision. It contains all cone cell types with the various color opsin pigments. It also contains a central 400 μm area devoid of retinal capillaries, which is called the foveal avascular zone. This foveal avascular zone is likely vascularized in utero but becomes nonvascularized shortly before birth. The exact center of the fovea is the foveal pit, also called the umbo (Miller 2006; Thumann et al. 2006; Schubert 2009). In this region, the retina is very thin, and no neurons are present. Cone cells in this region are of minimal size with a hexagonal shape and a very high density of approximately 200,000 cells per mm^2. No blue cones are present in the umbo, probably because they are large, susceptible to chromatic aberration from the lens, and consequently have low visual acuity potential. Rods are likewise absent, probably because they also have low visual acuity potential. Retinal pigment



Fovea, Foveal Avascular Zone (FAZ), Fig. 1 Fluorescein angiography demonstrating fovea and foveal avascular zone

epithelial cells in the fovea are taller, more narrow, and contain more pigment than retinal pigment epithelial cells in other areas of the fundus (Miller 2006). Surrounding the umbo, various structures radiate away through the retina in an oblique fashion, including cone axons and Henle fibers. All of these findings in the fovea likely represent evolutionary adjustments to maximize visual acuity by minimizing the amount of light and image scatter that occurs as photons traverse the retinal layers before reaching the photoreceptors (Fig. 1).

Cross-References

- ▶ Color Vision, Three Cone Opsins
- ▶ Retina, Structure of

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Foveola

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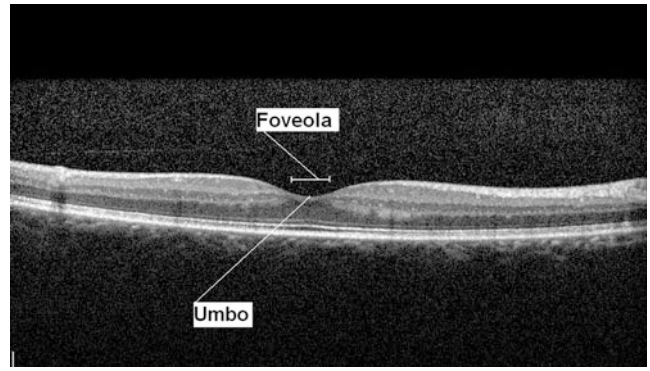
Definition

The anatomic central floor of the fovea.

Basic Characteristics

The foveola is the anatomic central floor of the fovea (Gass 1997; Gunton et al. 2005; Schubert 2009). It measures approximately 350 μm in diameter, lies within the foveal avascular zone, and contains the foveal pit (umbo). Since the foveola is located in the center of the fovea, the retina here is thin (only approximately 150 μm thick) and displays no overlying retinal ganglion cells. The geometrical center of the foveola is called the foveal pit or umbo. This is where maximal visual acuity is achieved with photoreceptors in this region, predominantly cone cells, being packed together very tightly with a density as high as 385,000 cells per mm^2. Their inner segments are linked together as the external limiting membrane of the retina, and their inner fibers and axons travel radially and peripherally as fibers of Henle in the outer plexiform layer. Peripheral to the foveola, retinal



Foveola, Fig. 1 Optical coherence tomography of fovea demonstrating foveola and umbo

thickness slopes upward as nuclei of the second- and third-order neurons along with those of Mueller cells appear. Retinal pigment epithelium cells directly under the foveola are taller, narrower, and contain more melanin granules per unit than elsewhere in the fundus (Yanoff and Fine 2002).

Development of the foveola begins very early in gestation with retinal cell division ceasing by 14 weeks gestational age. At 32 weeks gestational age, a depression in the retina appears as ganglion cells and inner retinal layers migrate peripherally. A single layer of ganglion cells and inner retinal layers is often still present at birth. This may explain the generally poor vision of neonates. Foveola formation usually completes by 11 months through 15 months postterm, at which time the ganglion and inner retinal cells have completely migrated out of the fovea. Maturation of the foveola continues over the subsequent 30 months as cone cells increase their densities by becoming longer and thinner, as well as pushing rod cells peripherally (Gunton et al. 2005).

A reduced foveola depression can be due to various developmental abnormalities, retinal diseases, or retinal dysplasias. Conditions associated with foveolar developmental aplasia or hypoplasia include albinism, aniridia, achromatopsia, X-linked hemeralopia, and microphthalmos. Foveola hypoplasia can also occur as an isolated condition (Querques et al. 2009). The foveolar depression can become blunted in the presence of retinal edema from various retinal vascular disorders, including diabetes, retinal vein occlusion, hypertensive retinopathy, and uveitis, among others. Foveola depression can also be distorted or blunted in cases of vitreomacular traction. Finally, foveomacular dysplasias can develop secondary to retinal colobomas and congenital toxoplasmosis (Yanoff and Fine 2002).

Retinal-vitreous attachments in the center of the fovea are very strong due to a thin internal limiting membrane. This logically explains the tendency for macular hole formation during periods of forceful anterior-posterior vitreous traction (Gass 1997; Yanoff and Fine 2002) (Fig. 1).

Cross-References

- ▶ Fovea, Foveal Avascular Zone (FAZ)
- ▶ Macular Holes
- ▶ Retina, Structure of

References

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Foville Syndrome

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Definition

Foville syndrome was initially described by Achille-Louis-Francois Foville, a French physician, in 1859 (Brogna et al. 2012). The crossed syndromes have been variously described and sometimes have conflicting or overlapping features in the literature. For this chapter, we use the definitions of Millard-Gubler (nuclear facial palsy and contralateral hemiparesis), Foville (facial palsy, conjugate horizontal gaze paralysis, and contralateral hemiparesis), Weber (oculomotor palsy and contralateral hemiparesis), and Raymond-Cestan (internuclear ophthalmoplegia and contralateral hemiparesis) that were abstracted from the original reports by Silverman et al. (1995). These syndromes demonstrate important principles in brainstem localization including cranial neuropathies contralateral to hemibody motor or sensory disturbances, medial longitudinal fasciculus and internuclear ophthalmoplegia, horizontal nuclear conjugate gaze palsies, and the corticobulbar innervation of the facial nerve nucleus.

Causes

It is caused by a unilateral lesion located in the dorsal pontine tegmentum in the caudal third of the pons (e.g., occlusion of a pontine branch of the basilar artery, tumors in the dorsal pons, hemorrhage, or demyelination) (Liu et al. 2010).

Presentation (Liu et al. 2010; Kline and Foroozan 2013; Neuro-Ophthalmology, BCSC/American Academy of Ophthalmology)

1. Ipsilateral horizontal gaze palsy (from nucleus of VI or parapontine reticular formation (PPRF))
2. Ipsilateral CN VII facial palsy
3. Contralateral hemiparesis (corticospinal tract)

Reference

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Kline LB, Foroozan R (2013) Neuro-ophthalmology, review manual, 7th edn. Slack Incorporated, Thorofare
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Neuro-Ophthalmology, BCSC/American Academy of Ophthalmology, Section 5, Edition 2013–2014
Silverman IE, Liu GT, Volpe NJ, Galetta SL (1995) The crossed paralyses. The original brain-stem syndromes of Millard-Gubler, Foville, Weber, and Raymond-Cestan. Arch Neurol 52(6):635–638

Franceschetti Hereditary Recurrent Erosion

▶ Recurrent Corneal Erosion

Franceschetti-Zwahlen-Klein Syndrome

▶ Treacher Collins-Franceschetti Syndrome (Mandibulofacial Dysostosis)

Francois Dyscephalic Syndrome

► Oculomandibulofacial Dyscephaly (Hallermann-Streiff Syndrome)

François, Central Cloudy Dystrophy

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Synonyms

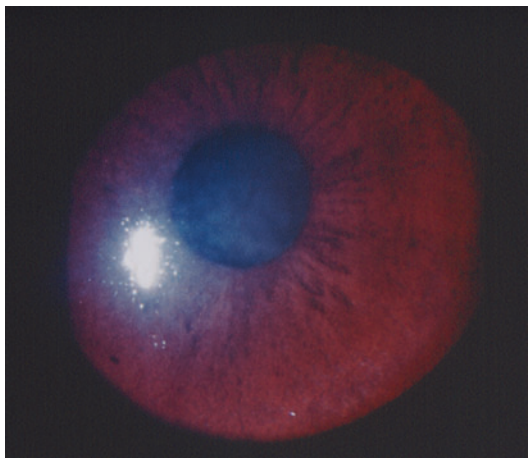
Central cloudy dystrophy of François

Definition

François disease is a nonprogressive bilateral corneal dystrophy characterized by central round opacities separated by clear linear areas (Figs.1, 2, and 3).

Etiology

Inheritance is autosomal dominant.



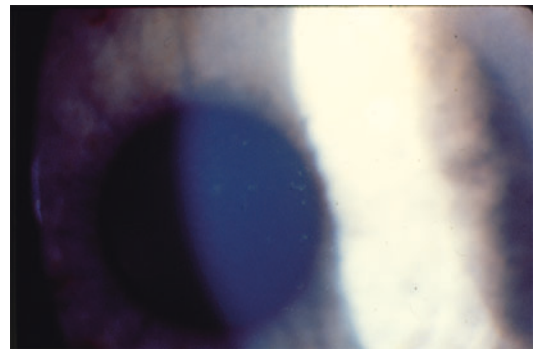
François, Central Cloudy Dystrophy, Fig. 1 Central polygonal opacities that fade peripherally

Clinical Presentation

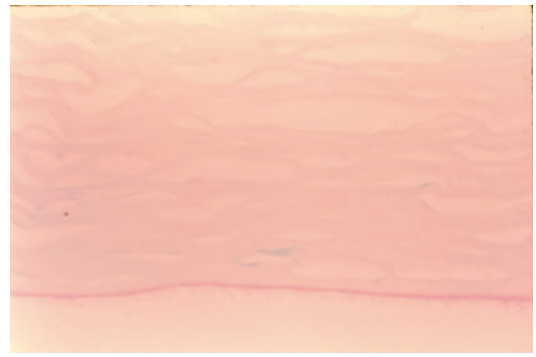
Patients are asymptomatic. Examination of the cornea reveals central polygonal opacities separated by clear lines and less prominent anteriorly and peripherally. The stroma is of normal thickness, erosion does not occur, and there is no loss of sensation. Appearance of the cornea is similar to crocodile shagreen (Krachmer et al. 2011).

Diagnostics

Light microscopy demonstrates staining of glycosaminoglycans and a rippling appearance of the deep stroma. Confocal microscopy can reveal highly refractile deposits in the anterior stroma with multiple dark striae in the posterior stroma (Weiss et al. 2008).



François, Central Cloudy Dystrophy, Fig. 2 Higher magnification of opacities



François, Central Cloudy Dystrophy, Fig. 3 Light microscopy demonstrating glycosaminoglycan deposition

Differential Diagnosis

Differential diagnosis includes corneal edema, posterior crocodile shagreen, fleck corneal dystrophy, posterior amorphous corneal dystrophy, pre-Descemet corneal dystrophy, and congenital hereditary stromal dystrophy.

Prophylaxis

There is no known prophylaxis.

Therapy

Patients are generally asymptomatic and treatment is not necessary required (Krachmer et al. 2011).

Prognosis

Prognosis is good and patients do not experience any pain or vision loss.

Epidemiology

The inheritance is autosomal dominant. The condition is rare and the exact prevalence is unknown.

Cross-References

- ▶ Congenital Hereditary Stromal Dystrophy
- ▶ Corneal Dystrophy
- ▶ Corneal Edema
- ▶ Posterior Amorphous Corneal Dystrophy

References

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Fraser-François Syndrome

▶ Cryptophthalmos-Syndactyly (Fraser) Syndrome

Freckle

▶ Ephelis (Freckle), of the Eyelid
▶ Ephelis (Freckle), Conjunctival Disease

F

Free Caps, LASIK Complication

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Synonyms

Free flaps

Definition

A free cap is a complication of LASIK in which instead of a flap with hinge, there is a complete resection of the flap. Usually this occurs due to unintended complete section or loss of suction.

Immunohistochemistry

As free caps are caused by mechanical factors (microkeratomes), no immunohistochemical process is involved.

Differential Diagnosis

Every other LASIK complication includes incomplete cuts, buttonholing, flap perforation, epithelial defects, wound dehiscence, irregular ablation, flap wrinkling, or slicing.

Cross-References

▶ Posterior Optic Buttonholing

Further Reading

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Free Conjunctival Autograft Transplantation

▶ Conjunctival Autograft

Free Conjunctival Transplant

▶ Conjunctival Autograft

Free Flaps

▶ Free Caps, LASIK Complication

Free Radical Damage

▶ Light Toxicity, Free Radical Damage; Photic Damage/Phototoxicity, Free Radical Damage

Free Radicals

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Definition

Free radicals are atoms, molecules, or ions with unpaired electrons that may have positive, negative, or zero charge. They influence many biological processes – some of them are essential for life, while others may lead to cell damage and death. The free radical theory of aging assumes that accumulation of free radical cell damage over time leads to mutation, cancer, and aging (Muller et al. 2007).

Structure

Pigmented molecules absorb visible and ultraviolet light which changes their energy level and leads to an electron loss. A free radical forms when a neighboring molecule gains this extra electron. In case of oxygen, the new molecule is called superoxide (Miller and Scott 2004).

Function

Free radicals may disrupt cell and mitochondrial membranes and nucleic acid and destroy tissue (Miller and Scott 2004). Fortunately, antioxidants such as superoxide dismutases, catalases and peroxiredoxins, glutathione, and vitamin C and E function as scavengers and protect molecules, cells, and tissues from oxidative damage (Miller and Scott 2004; Gutteridge and Halliwell 2010).

Clinical Relevance

Different tissues can develop light damages, depending on the light wavelength (mainly ultraviolet), intensity, and exposure time (Miller and Scott 2004):

1. Lid: epidermal keratoses; malignant skin changes
2. Cornea: superficial punctate keratitis (snow blindness); spheroidal degeneration
3. Lens: cataract
4. Retina: maculopathy

Cross-References

- ▶ Cataract, Causes and Treatment
- ▶ Keratitis

References

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Muller FL, Lustgarten MS, Jang Y, Richardson A, Van Remmen H (2007) Trends in oxidative aging theories. Free Radic Biol Med 43:477–503, Review

French Disease

- ▶ Syphilis: Overview

Frequency of Light Wave

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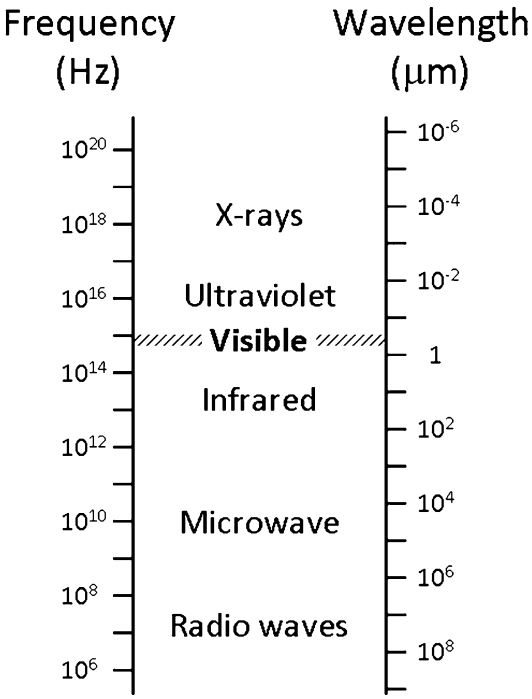
Synonyms

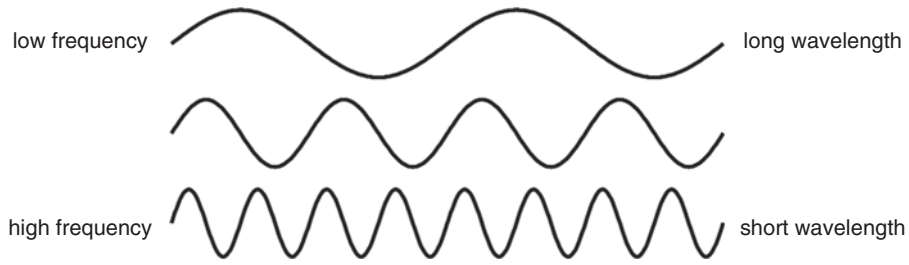
Electromagnetic spectrum; Inversely proportional to wavelength

Definition

Frequency is generally defined as the number of cycles per unit time. Figure 1 illustrates sinusoidal waves of various frequencies in cycles per second. The unit for temporal frequency is Hertz (Hz) or cycles per second. In optical physics, frequency refers to the rate of oscillation of the electromagnetic field per unit second. The electromagnetic spectrum is shown in Fig. 2. Frequency is mathematically defined as follows:



Frequency of Light Wave, Fig. 2 The electromagnetic spectrum



Frequency of Light Wave, Fig. 1 Illustration of sinusoidal waves with frequencies scaling by factors of 1, 2, and 4 (from *top* to *bottom*)

$$v = \frac{c}{\lambda}$$

where ν is the frequency, λ is the wavelength, and c is the speed of light in a vacuum (approximately 3×10^8 meters per second).

Cross-References

▶ Dispersion: Definition

Fresnel

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Definition

Augustin Jean Fresnel (pronounce *freɪˈnɛl*) was born on 10 May 1788 in Broglie (†14 July 1827 in Ville-d'Avray near Paris) and was a French Physicist and Engineer, who gave a major impact on wave theory of light and optics. A series of terms are named after Fresnel, e.g., Fresnel lens, Fresnel prism, and Fresnel diffraction theory (or Fresnel formulas). The Fresnel lens reduces the amount of material required compared to a conventional lens by dividing the lens into a set of concentric annular sections with stepwise discontinuities in between.

Cross-References

▶ Fresnel Prisms

Fresnel Prisms

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Definition

Fresnel (pronounce *freɪˈnɛl*) prisms are constructed as a series of very narrow adjacent prisms on a thin sheet typically made of plastic. The advantages to using Fresnel prisms are that they are lightweight and very convenient to use. They are available in powers of 1–40 prism diopters and due to flexibility it can be placed over conventional lenses. One disadvantage of Fresnel prisms is that higher-power prisms (more than 10–12 prism diopters) introduce glare and chromatic aberration.

Cross-References

▶ Fresnel

Frontoethmoidal Incision, for Anterior Orbitotomy

▶ Lynch Incision, for Anterior Orbitotomy

Fuchs Dystrophy

▶ Endothelial Degenerations

Fuchs Endothelial Corneal Dystrophy (FECD)

▶ Corneal Dystrophies

Fuchs Heterochromic Iridocyclitis, Glaucoma

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Synonyms

Uveitic glaucoma; Uveitis, iridocyclitis

Definition

Fuchs heterochromic iridocyclitis (FHI) is a unilateral condition characterized by mild anterior uveitis, iris heterochromia, cataract, and glaucoma. FHI remains a clinical diagnosis without any well-established diagnostic test.

Etiology and Mechanism

The exact etiology of FHI remains unknown, but several associations have been proposed (Allingham et al. 2005). Decreased innervation to iris stroma with resultant hypopigmentation and the presence of Horner's syndrome in some patients with FHI suggest the possibility of sympathetic dysfunction as an underlying etiology. A possible link with toxoplasmosis has also been proposed from studies reporting the presence of chorioretinal scars in a significantly higher proportion of eyes with FHI; however, no evidence by cellular immunity, enzyme-linked immunosorbent assays, or immunofluorescence antibody tests has been found. In one study measuring IgG antibodies against rubella, herpes simplex virus, varicella zoster virus, or *Toxoplasma gondii* in 46 patients, 13/14 patients with FHI had intraocular antibody production against rubella only, and none of the controls had positive rubella titers. Consequently, the authors proposed an association between rubella and FHI (de Groot-Mijnes et al. 2006).

The mechanism of secondary glaucoma in FHI is thought to be similar to that of chronic open-angle glaucoma, given an open and normal-appearing angle on gonioscopy. In other cases, active trabeculitis with various types of inflammatory cells may cause obstruction of aqueous outflow facility. Fine rubeotic vessels have been described in the angle and histology reports have indicated sclerosis of the trabecular meshwork and presence of an inflammatory membrane over the angle. Other mechanisms include lens-induced glaucoma, steroid-induced glaucoma, and secondary angle-closure glaucoma from peripheral anterior synechiae (Salim and Shields 2008).

Epidemiology

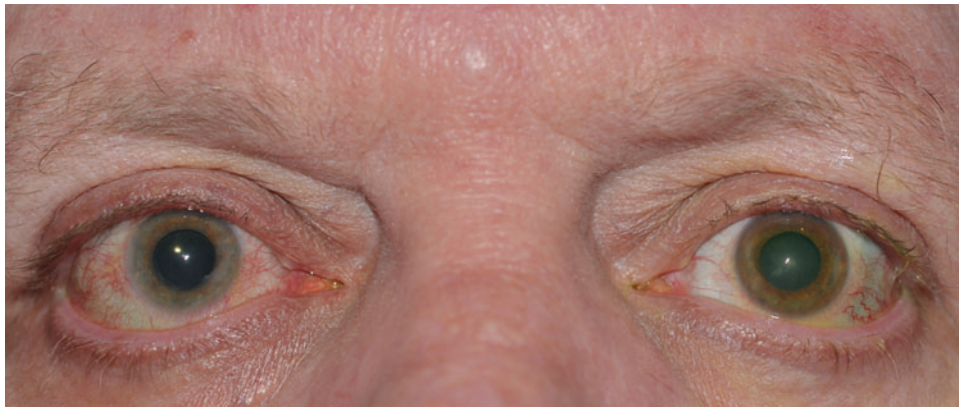
The prevalence of FHI is reported to be 2–11% of all uveitides. It usually presents in the third or fourth decade of life. There is no race or sex predilection. Glaucoma is the most sight-threatening complication of FHI with a prevalence of 9–59%.

Clinical Presentation

FHI, reportedly the most underdiagnosed form of iridocyclitis, typically lacks the usual symptoms of inflammation, including pain, photophobia, and redness. Patients may remain asymptomatic for many years and often present with reduced vision secondary to cataract formation. Glaucoma often presents as a late complication of FHI.

Clinical Examination

Iris heterochromia (Fig. 1) is present in a majority of patients, with the lighter-colored iris usually, but not invariably, being the affected eye. Iris heterochromia is more difficult to detect in dark-complected individuals. Iris nodules, both Koeppe and Busacca, may be present and may cause diagnostic confusion with other uveitides.



Fuchs Heterochromic Iridocyclitis, Glaucoma, Fig. 1 Iris heterochromia (lighter iris) and pseudophakia in an eye affected with FHI

Keratic precipitates (KP) tend to involve the entire endothelial surface of the cornea and appear fine and stellate. Iridocyclitis is mild with minimal flare and cells and runs a protracted course. Posterior synechiae are often absent, which helps differentiate FHI from other uveitides. Posterior subcapsular cataract formation is common in the affected eye. Glaucomatous optic nerve cupping and associated visual field loss may be seen with uncontrolled intraocular pressure (IOP). The drainage angle is open on gonioscopy in most cases. Posterior segment findings, including chorioretinal lesions and vitritis, may be present.

Differential Diagnosis

The main differential diagnosis is Posner-Schlossman syndrome or glaucomatocyclitic crisis, characterized by unilateral IOP spikes with mild anterior chamber inflammation. These eyes may also have a certain degree of heterochromia but often have higher IOP elevations. Unlike FHI, the inflammation in this condition responds to corticosteroid therapy with resolution of elevated IOP spikes. Herpes simplex uveitis (and other uveitides) should be considered as it may present with iris heterochromia and inflammation with diffuse KP. Other causes of iris heterochromia include Waardenburg's syndrome, congenital Horner's syndrome, and ocular melanosis and should also be ruled out.

Management and Prognosis

Iridocyclitis does not respond to corticosteroid therapy with most patients generally having a good prognosis despite persistent low grade inflammation. A short course of steroids may be used to differentiate FHI from Posner-Schlossman syndrome, but long-term use is not recommended. The outcomes of cataract extraction are reported to be equivalent or better in FHI when compared with other forms of chronic uveitides. Glaucoma management is challenging with 73% of cases failing with maximal medical therapy (La Hey et al. 1993). Laser trabeculoplasty is ineffective in these eyes, given the underlying inflammation and alterations in the angle anatomy from peripheral anterior synechiae, neovascularization of the angle, or presence of an inflammatory membrane covering the angle recess (Salim and Shields 2008). Glaucoma filtration surgery, even with antimetabolites, has limited success over time because of excessive scarring. Glaucoma drainage implants have higher success rates and are the preferred initial surgical intervention (Sung and Barton 2004). The course of glaucoma is not altered by cataract extraction.

Cross-References

- ▶ Intraocular Pressure
- ▶ Uveitic Glaucoma
- ▶ Uveitis in Multiple Sclerosis
- ▶ Uveitis, Iridocyclitis

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Fuchs Superficial Marginal Keratitis

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Definition

Bilateral inflammatorydisorder that results in progressive peripheral corneal thinning and pseudopterygium formation (Bierly et al. 1992; Brilakis et al. 2004).

Clinical Presentation

Patients usually present in the second to fourth decade of life. They classically complain of intermittent and recurrent episodes of ocular irritation and photophobia (Bierly et al. 1992). On exam, corneal inflammation with associated stromal thinning and marginal infiltrates are found. This stromalysis may quiet with time or progress to perforation (Goldberg et al. 1996). Pseudopterygium formation usually results once the inflammation has resolved (Kotecha and Raber 2001; Keenan et al. 2011). These patients usually have decreased visual acuity related to irregular astigmatism, which will require hard contact lens for correction.

Diagnosis

Clinical evidence of corneal thinning, inflammation, and neovascularization is typical. Given the rarity of this disease, it must be viewed as a diagnosis of exclusion. Patients should be worked up for systemic vasculitis, collagen vascular disease, severe dry eye, and infectious keratitis. Once infectious keratitis and autoimmune diseases have been ruled out, then this can be considered as a diagnosis.

Differential Diagnosis

1. Mooren's ulcer
2. Peripheral ulcerative keratitis
3. Terrien's marginal degeneration

Therapy

Visual rehabilitation can be done with glasses or hard contact lens (scleral lens may be required). Observation is the mainstay of treatment unless the globe integrity is becoming compromised. Immunosuppression with systemic or topical therapy can be considered in cases with significant ocular inflammation and patient discomfort (Kotecha and Raber 2001; Keenan et al. 2011). Treatment with vitamin C and doxycycline has been proposed as a way to slow down stromalysis and corneal thinning (Keenan et al. 2011).

If perforation is impending, tectonic patch grafting can be performed with cornea or corneoscleral patches (Bierly et al. 1992; Kotecha and Raber 2001; Brilakis et al. 2004; Keenan et al. 2011). Recurrences can occur after grafting.

Prognosis

Patients lead a quality of life comparable to the general population and most retain good vision as the central cornea is spared. Only in the severe cases do patients typically lose lines of best corrected visual acuity.

Epidemiology

Rare

Cross-References

► Terrien Marginal Degeneration

References

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Fuchs' Corneal Dystrophy

► Fuchs' Dystrophy Disease

Fuchs' Dystrophy Disease

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Synonyms

Endoepithelial corneal dystrophy; Fuchs' corneal dystrophy; Fuchs' endothelial corneal dystrophy; Late hereditary endothelial dystrophy

Definition

Fuchs' dystrophy is a progressive, late-onset degeneration of the cornea characterized by focal excrescences of Descemet's membrane known as *guttae*, resulting in loss of endothelial barrier function, stromal edema, and, in late stages, painful epithelial bullae (Waring et al. 1978; Reinhard and Larkin 2008; Lisch and Seitz 2011).

Etiology

Corneal decompensation in Fuchs' dystrophy originates in disease of the corneal endothelium and subsequent misregulation of fluid balance within the cornea. Causative genetic mutations coding for an ion cotransporter (SLC4A11), a transcription control factor (TCF8), a lipoxygenase (LOXHD1), and an intronic variant in TCF4 have been identified, but the precise pathogenic process has yet to be identified. Hereditary transmission is multifactorial and often autosomal dominant, with severe disease phenotype associated with acquisition of a disease allele from both parents (Waring et al. 1978; Reinhard and Larkin 2008; Lisch and Seitz 2011).

Clinical Presentation

Patients initially present with bilateral, painless blurry vision upon waking that improves during

the day. It is most commonly identified in females of middle age. Slit-lamp biomicroscopy reveals central guttae in early stages which coalesce and develop in the periphery over time. The development of corneal edema correlates with progression in a number of guttae (Waring et al. 1978; Reinhard and Larkin 2008; Lisch and Seitz 2011).

Diagnosis

Diagnosis of Fuchs' dystrophy is primarily made by the identification of guttae with slit-lamp biomicroscopy. The presence of guttae and endothelial cell density attenuation can be confirmed with specular microscopy. Corneal pachymetry is a useful modality to follow progression and severity as edema increases over time (Waring et al. 1978; Reinhard and Larkin 2008; Lisch and Seitz 2011).

Differential Diagnosis

Posterior polymorphous corneal dystrophy and iridocorneal endothelial syndrome present with punched out lesions or beaten-metal appearance of the corneal endothelium which may be confused for guttae. The eyes with posttraumatic deposition of pigment on the corneal endothelium, anterior uveitis, and herpetic keratouveitis may also present with a similar appearance.

Corneal edema and epithelial bullae are characteristic features of aphakic or pseudophakic bullous keratopathy. Interstitial keratitis presents with corneal edema but with increased vascularity; Fuchs' dystrophy is by nature not an inflammatory disease (Waring et al. 1978; Reinhard and Larkin 2008; Lisch and Seitz 2011).

Prophylaxis

There are no clinically proven methods of prophylaxis for Fuchs' dystrophy. Smoking increases the risk of development of corneal guttae and should be avoided (Waring et al. 1978; Reinhard and Larkin 2008; Lisch and Seitz 2011).

Therapy

Medical management of Fuchs' dystrophy addresses symptoms of corneal edema and painful bullae and consists of topical hypertonic saline, hairdryer use to dehydrate the precorneal tear film, and therapeutic soft contact lenses.

Definitive treatment of disease is surgical. Penetrating keratoplasty, historically the mainstay of treatment, has given way in the past decade to endothelial keratoplasty. Descemet's stripping endothelial keratoplasty and Descemet's membrane endothelial keratoplasty allow a more stable intraoperative anterior chamber and faster postoperative healing (Waring et al. 1978; Reinhard and Larkin 2008; Lisch and Seitz 2011).

Prognosis

Endothelial cell loss, formation of guttae, and development of corneal edema are gradual processes that progress over years, with family studies showing an average of 20 years from identification of mild disease to diffuse corneal decompensation (Waring et al. 1978; Reinhard and Larkin 2008; Lisch and Seitz 2011).

Epidemiology

Regions of highest prevalence with Fuchs' dystrophy include North America and Europe, at approximately 4% of individuals over 40 years of age. Significantly lesser frequency of disease is seen in Asia and South America. While mild disease is seen with the above frequency, only 0.1% experience epithelial edema and bullae formation (Waring et al. 1978; Reinhard and Larkin 2008; Lisch and Seitz 2011).

Cross-References

► Endothelial Dystrophy

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Fuchs' Endothelial Corneal Dystrophy

▶ Fuchs' Dystrophy Disease

Fuchs' Uveitis Syndrome (FUS) with Secondary Glaucoma

▶ Heterochromic Cyclitis Fuchs' Glaucoma

Full-Thickness Eyelid Biopsy

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Synonyms

Biopsy; Lid biopsy

Definition

Removal of a complete section of the eyelid by incising all layers.

Indication

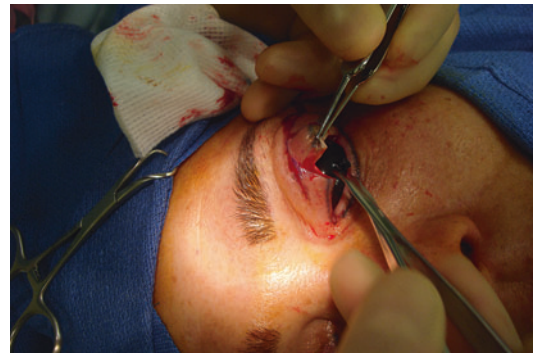
To fully remove a lesion while achieving proper cosmetic repair and to maintain normal lid margin architecture. Typically full thickness eyelid biopsy is performed when a lesion involves or is in close proximity to the eyelid margin, and removal of the lesion alone would result in an eyelid defect such as a notch or keratinization past the normal mucocutaneous junction.

Contraindication

Tumors that are very superficial or far from the eyelid margin may be poor candidates for full thickness eyelid biopsy. Additionally, for medial eyelid tumors, full thickness procedures risk damage to the canaliculi and lacrimal drainage apparatus.

Techniques and Principles

The tissue surrounding the lesion is anesthetized with local anesthetic with epinephrine. A scalpel or scissors is used to incise the eyelid full thickness on either side of the lesion. The vertical extent usually extends completely through the tarsus to avoid lid contour abnormalities on closure (Fig. 1). Typically, a pentagonal excision pattern is employed around the lesion. This type of excision pattern allows for a proper approximation of the lid edges resulting in satisfactory cosmetic repair. A rim of normal tissue, around



Full-Thickness Eyelid Biopsy, Fig. 1 Intraoperative photo of full thickness excision

1-5 mm (depending on the level of suspicion for malignancy), is usually included in an attempt to fully excise the lesion (Nerad 2001; Albert and Jakobiec 2008).

Outcomes

Excellent aesthetic and functional results are achieved with proper pentagonal wedge procedures. The lesion may be removed completely, theoretically increasing the likelihood of a cure if the lesion is malignant.

Complications

Bleeding and blood loss may occur since the marginal arcades are usually violated. Also meticulous margin approximation is necessary to avoid lid margin contour abnormalities. Usually, only up to one third of the lid extent may be closed primarily. Larger defects may need more advanced closure techniques.

Cross-References

► Excisional Biopsy

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Functional

► Nonorganic Visual Loss

Functional Ptosis

► Pseudoptosis

Fundamental Considerations Regarding the Optic Nerve

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Synonyms

Optic disc; Optic nerve head; Papilla nervi optici

Definition

The optic nerve head (papilla nervi optici) is the visible part of all those retinal ganglion cell fibers conglomerating as a bundle and leaving the eye. The optic nerve fibers penetrate the sclera through multiple perforations of varying sizes, known as the lamina cribrosa (sieve sheets). Behind the globe, the fibers continue as the myelinated optic nerve, surrounded by meninges along its passage through the orbit and up where the optic nerves cross (optic chiasm). The optic nerve head is divided into four parts: the nerve fibers, the prelaminar, laminar, and retrolaminar parts.

The Optic Nerve Head = The Papilla

Various parameters need to be evaluated:

1. Size/area. The size/area of the papilla varies between individuals, and is defined as the tissue within the borders of Elschnig's scleral ring. In Caucasians, the area ranges from 1.6 to 2.8 mm^2. Smaller optic nerves are described as micropapillae, larger ones as macropapillae. The size is important, because it is always compared to the size of the excavation (or cup) of the optic nerve head. Small papillae may have no or only a very small excavation, whereas large papillae often also have larger excavations, without pathological changes being present. A narrow scleral canal in small optic nerve heads can lead to an indistinct

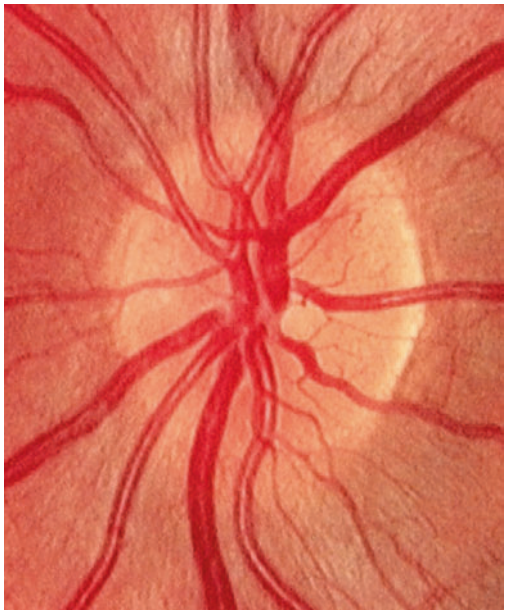
border, and a crowded disc. The size of the papilla is also dependent on ethnicity: Africans and Afro-Caribbeans have larger papillae on average.

2. Shape. A normal optic nerve head is vertically oval. A skew torted disc is a rotation of >15°, and a tilted disc is a disc with an angulation in the anterior-posterior axis. These findings are common in high myopia, often in combination with astigmatism and/or amblyopia.
3. Neuroretinal rim-size/-area. The papilla can have a central excavation, which remains stationary, and is considered physiological. The shape of this excavation is round to slightly horizontally oval. The size of the excavation determines the neuroretinal rim: Total disc area – excavation area. The vertical and horizontal diameter of the excavation is compared with the respective diameters of the optic disc, and a quotient of excavation vs. papillary diameter, or cup/disc ratio, is determined. The neuroretinal rim must be intact around the circumference of the disc, and in healthy subjects often demonstrates the following characteristic: Broadest inferiorly, followed by superior and nasal, and narrowest temporally. The first letters of the mentioned areas form the "ISNT"-rule: if this rule is followed, then glaucoma damage *isn't* present. There is also an ISNT-light: Inferior may not be narrower than superior. Only 5% of the population have a C/D ratio of >0.6. An asymmetry of the cup/disc ratio of >0.2 should raise suspicion of glaucoma. The excavation in glaucoma enlarges from the inner, central side, either concentrically, or more often, supero- or inferotemporally as a notch. Vertical cup-disc ratio and size of the disc are highly heritable. Instead of the cup/disc ratio, the rim/disc ratio (radial width of the neuroretinal rim at its thinnest point compared to the diameter of the disc in the same axis) can be evaluated.
4. Color. The neuroretinal rim has a yellowish-pink appearance. Yellowing of the crystalline lens (cataract) may give a false yellow appearance of a pale disc. Occlusion of the fine blood vessels leads to a pale white appearance (i.e., optic atrophy due to vascular insufficiency, inflammation, or pressure from tumors)
5. Vessels. The central retinal artery and vein emerge from the center, or slightly superonasally of the papilla, and usually splits into four main branches to supply the four quadrants of the inner retina. In glaucoma, the vessels are shifted nasally. The loss of surrounding neuroretinal tissue can lead to the vessels lying free and forming a bridge to the disc margin. If the excavation leads to undermining of the margin, the vessels can take on a bayonet shaped kink.
6. Disc margin hemorrhages. These are microinfarctions and occur very rarely in healthy individuals (<2%). These hemorrhages are usually streak-like within one disc diameter of the disc margin, but can also occur within the disc. They are often found supero- or inferotemporally. These bleeds can be easily missed, and must be looked for actively. Red free light will show them up as dark streaks which are more readily visualized. After approximately 2 months they have disappeared. In glaucoma they are seen more often (4% in primary open-angle glaucoma, 40% in normal tension glaucoma), and are pathognomonic for progression of glaucoma damage. If the neuroretinal rim has been lost, no more disc hemorrhages will occur.
7. Peripapillary tissue. Tissue atrophy usually occurs temporally, but can also be circumferential. The so-called beta zone is an atrophy of receptor cells, retinal pigment epithelium, and small choroidal vessels at the edge of the disc. The alpha zone lies peripheral to this, with hyper- or hypopigmentation. The beta zone can enlarge in glaucoma.
8. Retinal nerve fiber layer. The neurons of all retinal ganglion cells congregate towards the optic disc and follow an arcuate path. A horizontal raphe forms the border between superior and inferior fibers. The longer the fiber, the deeper it lies. In glaucoma, the fibers can undergo generalized or sectoral decrease, which can be demonstrated as wedge shaped defects from the disc margin with red free light.

Lamina Cribrosa

The lamina cribrosa is formed by connective tissue and is regarded as the main site of glaucoma damage, since the retinal nerve fibers make a 90° bend at the disc margin, and then move through the pores of the lamina cribrosa, which are slightly offset. The pores have different sizes: usually larger superiorly and inferiorly, and thus possibly less support for the fibers. The lamina cribrosa is angled at the edge of the disc, and can change elastically, depending on intraocular and intracranial pressure, bending forward or backward, creating stress and strain. With age the elasticity decreases. This can impair the axoplasmic flow in both directions.

The more atrophic the nerve fiber layer, the more pores become visible. The excavation thus does not only become wider, but deeper as well.



Fundamental Considerations Regarding the Optic Nerve, Fig. 1 Normal optic disc with centrally located vessels and no excavation (cup)

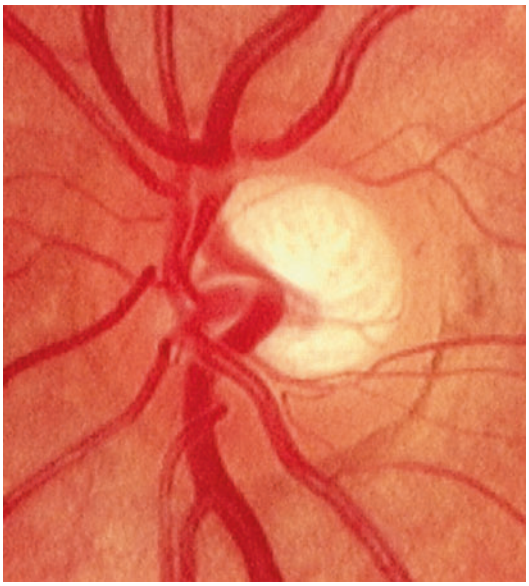
Drusen

Drusen are waste products of nerve fiber metabolism, which can become increasingly deposited if not adequately removed. They can occur superficially in the area of the nerve fiber layer or in the deeper prepapillary area. They are usually dynamic and can change size and position, and are commoner in smaller discs.

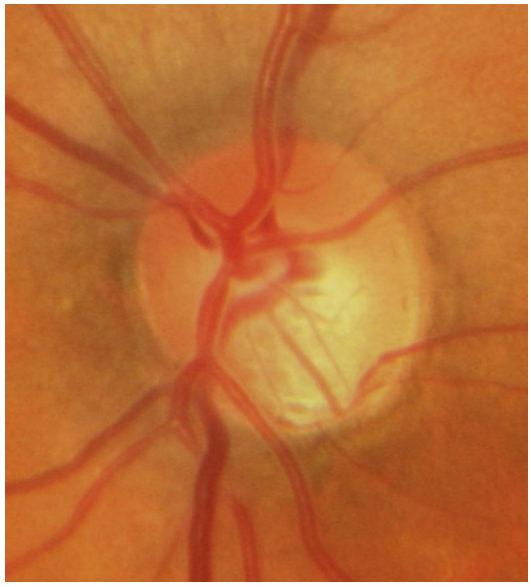
Congenital Malformations

The optic nerve forms as a protrusion of the brain. An incomplete closure of the optic cup leads to an inferior chorioretinal coloboma, and occasionally to an optic nerve coloboma as well. A giant "excavation" with all vessels seeming to arise from the disc margin, and the disc lying in the center, is described as a "morning glory" anomaly, due to the resemblance with a flower. Small deep defects are called optic pits, which can be associated with a canal towards the macular region, and lead to macular edema.

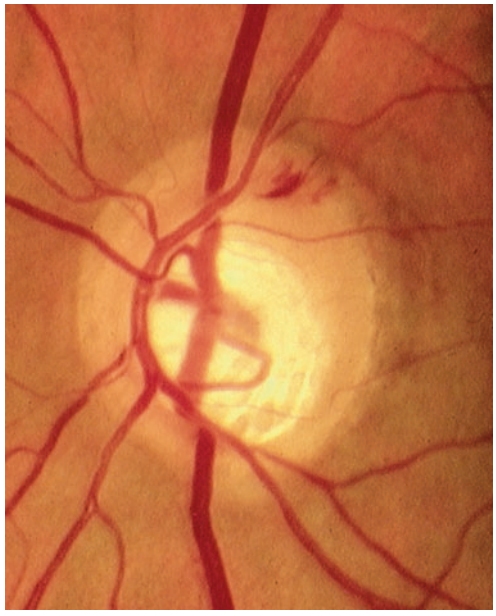
Remnants of embryonic material (glial tissue, Bergmeister papilla) or hyaloid arteries can be present.



Fundamental Considerations Regarding the Optic Nerve, Fig. 2 Normal optic disc fulfilling the ISNT rule: the neuroretinal rim is thickest inferiorly, followed by superiorly, nasally, and finally temporally



Fundamental Considerations Regarding the Optic Nerve, Fig. 3 Glaucomatous disc with loss of the neuroretinal rim (notch) from 5 to 6 o'clock



Fundamental Considerations Regarding the Optic Nerve, Fig. 4 Glaucomatous disc with loss of neuroretinal rim inferotemporally and a hemorrhage at 1 o'clock

A hypoplasia of the optic nerve is exceedingly rare. Too few nerve fibers are present.

Within the eye, nerve fibers are generally not myelinated. Rarely one can find myelinated fibers close to the disc, which are not pathological (Figs. 1, 2, 3, and 4).

Cross-References

- ▶ Angle-Closure Glaucoma
- ▶ Angle Closure Secondary to Uveal Effusion
- ▶ Angle-Closure Suspect
- ▶ Angle Recession Glaucoma
- ▶ Aqueous Humor
- ▶ Bergmeister's Papilla
- ▶ Drusen
- ▶ Ghost Cell Glaucoma
- ▶ Fuchs Heterochromic Iridocyclitis, Glaucoma
- ▶ Heterochromic Cyclitis Fuchs' Glaucoma
- ▶ High-Pressure Glaucoma
- ▶ Intraocular Pressure
- ▶ Juvenile Glaucoma
- ▶ Lens-Induced Angle-Closure Glaucoma
- ▶ Neovascular Glaucoma in Diabetes Mellitus
- ▶ Neovascular Glaucoma in Ocular Ischemia, Others
- ▶ Neovascular Glaucoma in VOR
- ▶ Open-angle Glaucomas
- ▶ Optic Disc (Optic Nerve Head)
- ▶ Optic Nerve Head Drusen
- ▶ Pediatric Glaucoma
- ▶ Posner-Schlossman Syndrome
- ▶ Primary Angle Closure and Angle Closure Glaucoma
- ▶ Primary Congenital Glaucoma
- ▶ Pseudoexfoliative Glaucoma
- ▶ Secondary Angle-Closure Glaucoma
- ▶ Secondary Glaucoma in Uveitis/Inflammatory Eye Disease
- ▶ Secondary Open-Angle Glaucoma
- ▶ Traumatic Glaucoma
- ▶ Uveitic Glaucoma

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Fundus Albipunctatus

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Synonyms

Fundus albipunctatus cum hemeralopia

Definition

Fundus albipunctatus is a rare autosomal-recessive form of congenital stationary night. First described by Lauber in 1910, fundus albipunctatus is remarkable for fundus exam findings showing many discrete white-yellow lesions deep in the retina. These distinct whitish-yellow lesions start in a ring-like formation around the macula and extending into the periphery. The macula itself is usually spared. Patients experience impaired night vision, but visual acuity, visual fields, and color vision are normal. Because nyctalopia is congenital, some patients may not even be symptomatic. Although the retinal lesions can change with time from a fleck-like appearance to a more numerous dot-like appearance, no retinal degenerative changes occur. Central visual acuity remains good into middle age. Approximately half of patients with fundus albipunctatus will develop a progressive cone macular dystrophy later in life, usually over the age of 40.

Fundus albipunctatus has distinctive electrophysiological findings. Dark adaptometry shows significantly delayed cone and rod adaptation but, given enough time, eventually reaches normal threshold. With full-field electroretinogram (ERG), the rod scotopic response after normal dark adaptation of 30–40 min is reduced. If dark adaptation is extended out to three to four times normal, the scotopic full-field ERG response normalizes. Photopic full-field ERG responses are normal or very mildly reduced unless cone macular dystrophy is present. Electroretinogram (ERG) responses with normal dark adaptation are also reduced but will normalize with prolonged dark adaptation.

Etiology

Some cases of fundus albipunctatus are caused by mutations in the RDH5 gene located on chromosome 12q13-14. The RDH5 gene encodes an enzyme, 11-cis retinol dehydrogenase, found in the retinal pigment epithelium (RPE) that is important in the conversion of 11-cis retinol to 11-cis retinal needed for the synthesis of rhodopsin. Impairment of 11-cis retinol dehydrogenase results in prolonged regeneration of visual pigment. Some patients have not been found to have mutations in RDH5 gene, suggesting other genes may also play a role in the development of fundus albipunctatus.

Occurrence

Fundus albipunctatus is a rare autosomal recessive disorder.

Classification

Fundus albipunctatus is classified as a subtype of congenital stationary night blindness (CSNB).

It is important to differentiate fundus albipunctatus from retinitis punctata albescens, a progressive tapetoretinal degeneration that has a very similar appearance in younger patients but is progressive and can result in blindness. Included in the differential diagnosis of fundus albipunctatus are canthaxanthine retinopathy, basal laminar drusen, cystinosis, oxalosis, and other causes of acquired nyctalopia such as vitamin A deficiency.

Cross-References

- ▶ Cone Dystrophies/Degeneration
- ▶ Crystalline Dystrophy
- ▶ Night Blindness
- ▶ Nyctalopia: Night Blindness
- ▶ Retina, Structure of

Further Reading

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Fundus Albipunctatus Cum Hemeralopia

- ▶ Fundus Albipunctatus

Fundus Coloboma

- ▶ Ectasia, Retinal

Fundus Flavimaculatus (Stargardt Disease/Juvenile Macular Degeneration)

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Synonyms

Juvenile macular degeneration; Juvenile macular dystrophy; Stargardt disease; Stargardt macular dystrophy

Definition

In 1909, Stargardt described a group of patients with bilateral atrophic-appearing changes within the macula with surrounding whitish-yellow flecks that extended out into the periphery. In 1963, Franceschetti used the term "fundus flavimaculatus" to describe a group of patients with fleck-like lesions in the retina with or without macular changes. The similarities of the fleck-like lesions with Stargardt disease and fundus flavimaculatus had led to discussion that the two diseases may actually be the same with overlapping clinical findings. However, some still use the term "Stargardt disease" to describe patients usually presenting at a younger age with atrophic macular changes with surrounding fleck-like lesions and "fundus flavimaculatus" to describe adult patients with fleck-like changes in the retina with no macular involvement.

If thought of as one disease, Stargardt disease/fundus flavimaculatus is probably best defined as a bilateral, autosomal recessive disease characterized by fleck-like lesions in the retina with or without atrophic macular changes and having a characteristic "dark choroid" on fluorescein angiogram.

Etiology

Mutations in the ABCR gene on chromosome 1 were identified in patients with Stargardt disease and fundus flavimaculatus in 1997. The ABCR gene encodes an ATP-binding cassette transporter protein, ABCA4, that is found in photoreceptor outer segments of both rods and cones. It is thought that this protein transports vitamin A derivatives across intracellular membranes. ABCR gene was renamed to the ABCA4 gene which stands for ABC cassette, subfamily A, member 4. The ABCA4 gene has significant sequence variability, with various heterozygotic sequences being disease causing for Stargardt disease/fundus flavimaculatus. Interestingly, other mutations in the ABCA4 gene have been shown to cause retinitis pigmentosa and cone dystrophies.

Clinical Presentation

Patients with Stargardt disease/fundus flavimaculatus usually present in the first or second decade of life with decreased central visual acuity, although this is variable. Dilated fundus exam may show subtle foveal pigmentary abnormalities sometimes described as a "beaten bronze appearance." Atrophic changes at the level of the retinal pigment epithelium (RPE) may also be present in the macula. Many patients have fleck-like lesions around the fovea that extend into the periphery. These fleck-like lesions have been described as linear, ovoid, or pisiform (fish-like) in shape and may change over time. As the retinal findings evolve, visual acuity usually deteriorates to about the 20/200 level, although this is variable.

Fluorescein angiography (FA) shows the characteristic finding of a "dark choroid" thought to be due to accumulation of lipofuscin at the level of the RPE which leads to blockage of normal choroidal fluorescence. A "bull-eye" type of fluorescence can sometimes be seen in the macula with central dark hypofluorescence surrounded by a ring of hyperfluorescent spots.

Electrophysiologic testing with full-field electroretinogram (ERG) shows variable responses ranging from normal to subnormal with impaired rod and cone responses.

Diagnosis

The diagnosis of Stargardt disease/fundus flavimaculatus is supported by a family history suggesting autosomal recessive inheritance pattern, clinical exam findings of fleck-like lesions with or without macular atrophy, and characteristic "dark choroid" findings and possible bull-eye-like macular changes seen on FA. Recently genetic testing for the ABCA4 gene has become available and also can help support the diagnosis of Stargardt disease/fundus flavimaculatus.

Differential Diagnosis

Differential diagnosis should include other disorders with flecked lesions of the retina such as drusen, multiple vitelliform lesions, fundus albipunctatus, and peau d'orange retinal findings seen with pseudoxanthoma elasticum.

Prophylaxis

Genetic testing and genetic counseling are available for those families affected by Stargardt disease/fundus flavimaculatus.

Therapy

No known treatments exist. Patients may benefit from low vision referral and genetic counseling.

Prognosis

Although variable, visual acuity usually stabilizes around 20/200 level.

Epidemiology

It is estimated that approximately 1 in 10,000 has Stargardt disease/fundus flavimaculatus.

Cross-References

- ▶ Angiography, Fluorescein
- ▶ Duchenne Muscular Dystrophy: Retinal Degeneration

Further Reading

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Fundus Oculi

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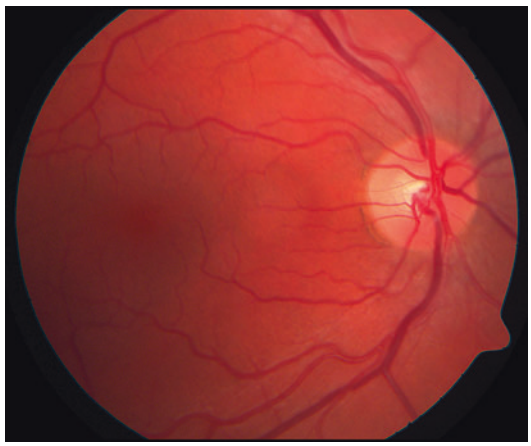
The interior concave portion of the eye, consisting of the retina, choroid, optic nerve head, and sclera as seen with the indirect ophthalmoscope (Fig. 1).



Fundus Oculi, Fig. 1 Fundus photograph demonstrating fundus oculi

Cross-References

- ▶ Indirect Ophthalmoscope
- ▶ Optic Disc (Optic Nerve Head)

Further Reading

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Fundus Salt and Pepper

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Synonyms

Pigmentary retinopathy

Definition

A disturbance or insult to the retina or retinal pigment epithelium (RPE) can result in pigmentary changes in the retina. Salt-and-pepper fundus is a nonspecific term to describe areas of hypopigmentation due to atrophic retinal changes (salt) with pigmentary alterations from pigment migration (pepper) in large portions of the retina. A number of disorders, dystrophies, infections, or toxicities can result in salt-and-pepper fundus changes.

Etiology

Salt-and-pepper pigmentary retinal changes can be seen with many ocular disorders. These include congenital infections, retinal dystrophies, systemic metabolic disorders, and ocular drug toxicities. Many of the severe pigmentary retinopathies are genetic in origin with onset seen in childhood:

Congenital/acquired infections:
- Rubella retinopathy secondary to congenital infection
- Syphilitic retinopathy secondary to congenital or acquired infection
- Diffuse unilateral subacute neuroretinitis (DUSN)
- Toxoplasmotic retinochoroiditis
- Herpetic retinopathies

Retinal dystrophies:
- Retinitis pigmentosa (rod-cone dystrophy)
- Leber congenital amaurosis
- Usher syndrome
- Goldmann-Favre syndrome

Systemic metabolic disorders:
- Bardet-Biedl syndrome
- Alström syndrome
- Refsum syndrome
- Abetalipoproteinemia (Bassen-Kornzweig syndrome)
- Neuronal ceroid lipofuscinosis

Systemic mitochondrial retinopathy:
- Kearns-Sayre syndrome
- Chronic progressive external ophthalmoplegia (CPEO)

Autoimmune paraneoplastic retinopathy:
- Cancer-associated retinopathy (CAR)
- Melanoma-associated retinopathy (MAR)

Drug toxicities – pigmentary changes can be seen with long-term use and/or high doses:
- Thioridazine
- Chlorpromazine
- Chloroquine
- Hydroxychloroquine
- Quinine

Trauma/postsurgical:
- Traumatic retinopathy due to old commotio retinae
- Pigmentary changes following retinal detachments

Occurrence

The onset of pigmentary changes is dependent on the etiology. Many causes of pigmentary retinopathies may have manifestations in childhood as seen with Leber congenital amaurosis or congenital rubella. Others may not develop until later in life such as changes from acquired syphilis or associated with CAR. Affected individuals may have other ocular symptoms such as nyctalopia, peripheral field loss, nystagmus, or impaired vision. Systemic changes may also be present with some disorders with pigmentary retinopathy. Many pigmentary retinopathies are slowly progressive.

Classification

Identifying the etiology of pigmentary alterations can be challenging. Electrophysiology can play a pivotal role in establishing a diagnosis. For example, electroretinograms (ERGs) will be severely affected in patients with Usher syndrome or Leber congenital amaurosis but normal or only mildly affected in congenital rubella. A detailed family, medical, and ocular history, a through ocular exam, and systemic evaluation for other manifestations that may be associated with systemic disorders may aid in the diagnosis. Directed lab studies may also help in diagnosis, for example, Refsum syndrome is characterized by abnormally elevated serum phytanic acid levels.

Cross-References

- ▶ Arteriohepatic Dysplasia (Alagille Syndrome), Retinal Degeneration
- ▶ Atypical Retinitis Pigmentosa (RP)
- ▶ Bardet–Biedl Syndrome, Renal
- ▶ Cancer-Associated Retinopathy (CAR)
- ▶ Chloroquine Toxicity, Cornea Verticillata
- ▶ Commotio Retinae (Berlin Disease/Edema)
- ▶ Kearns Syndrome
- ▶ Nyctalopia: Night Blindness
- ▶ Usher Syndrome

Further Reading

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Fungal Corneal Infection

► Candida Keratitis/Ocular Infection

Fungal Keratitis with Ulceration

► Ulcerative Keratitis Disease

Furrow Degeneration

► Furrow Degeneration, Senile

Furrow Degeneration, Senile

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Synonyms

Furrow degeneration; Idiopathic furrow degeneration; Senile furrow; Senile marginal atrophy; Senile marginal degeneration

Definition

Peripheral thinning is seen in the avascular zone between arcus senilis and the limbal vascular arcades (Farjo and Sugar (n.d.); Palay 2011; Tuft (n.d.)).

Etiology

Furrow degeneration is a corneal thinning in the periphery of the cornea that commonly occurs in association with arcus senilis. A fragmentation of peripheral corneal collagen results in a non-inflammatory depression at the corneal limbus (Farjo and Sugar (n.d.); Palay 2011; Tuft (n.d.)).

Clinical Presentation

Patients are typically asymptomatic. The corneal thinning is usually seen on routine eye exam between the corneal arcus and the limbus. The thinning is usually mild and there are no signs of inflammation or neovascularization. Occasionally the thinning can induce astigmatism.

Diagnosis

There is a zone of clearing between the corneal arcus and the corneal limbus (Tuft (n.d.)). The epithelium is intact and the cornea does not show any signs of neovascularization or inflammation (Farjo and Sugar (n.d.); Palay 2011; Tuft (n.d.)).

Differential Diagnosis

1. Terrien's marginal degeneration
2. Pellucid marginal degeneration
3. Dellen

Treatment/Prognosis

Asymptomatic. No treatment necessary unless significant astigmatism is induced.

Epidemiology

Incidence increases with age.

References

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G

GA

► Atrophy, Geographic

Gardner Syndrome: Retinal Pigment Epithelium Hypertrophy

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Synonyms

Familial adenomatous polyposis

Definition

Variant of familial adenomatous polyposis characterized by pigmented fundus ocular lesions, adenomatous polyposis of the small and large intestines, and other various neoplasms, including osteomas, fibromas, and desmoid tumors (Buettner 2006; Gass 1997; Humayun and Traboulsi 1999).

Etiology

Autosomal dominantly inherited mutation in the APC gene (tumor suppressor gene) located on the long arm of chromosome 5 (5q21) (Online Mendelian Inheritance of Man).

Clinical Presentation

Although over 80% of patients with Gardner syndrome have pigmented fundus lesions, the majority of patients are visually asymptomatic. Their pigmented fundus lesions are identified most often either during general routine ophthalmoscopy or during ophthalmic screening for familial adenomatous polyposis. Ophthalmoscopically, the pigmented fundus lesions of Gardner syndrome are flat, ovoid, variably pigmented subretinal lesions with a hypopigmented halo or depigmented tail. They can be differentiated from typical congenital hypertrophy of the retinal pigment epithelium (CHRPE) in the normal population by their smaller, more ovoid or pisciform, more variegated, multiple, and bilateral appearance. Histologically, the pigmented fundus lesions of Gardner syndrome are adenomas or hamartomas of retinal pigment epithelium since they can demonstrate multiple layers of abnormal hypertrophic retinal pigment epithelium cells. Occasionally, the abnormal hypertrophic cells of the pigmented fundus lesions occupy the full thickness of the retina (Fig. 1).

Patients with Gardner syndrome typically develop polyps in their small and large intestinal during their third decade of life. If left untreated,

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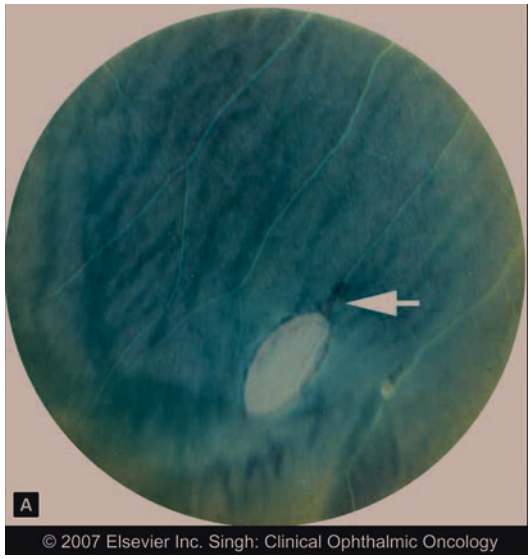

Gardner Syndrome: Retinal Pigment Epithelium Hypertrophy, Fig. 1 Color fundus photograph demonstrating pigmented fundus lesion characteristic for Gardner syndrome (From: Singh AD, Damato BE, Pe'er J, Murphree L, Perry JD (eds) (2007) Clinical Ophthalmic Oncology. Elsevier, Philadelphia. With permission)

the gastrointestinal polyps can progress to adenocarcinoma by the fifth decade of life.

Diagnostics

Pigmented fundus lesions of Gardner syndrome are best detected with a dilated fundus exam and scleral depression. Any abnormal pigmentation of the fundus should be documented with fundus photography. Lesions demonstrating thickness should be measured using ocular echography. If four or more lesions characteristic for the pigmented fundus lesions of Gardner syndrome are seen in one or both eyes, the patient should receive genetic studies looking for the APC mutation. Diagnosis of Gardner syndrome is confirmed by documenting adenomatous polyposis of the small and large intestine during either esophagogastroduodenoscopy or colonoscopy.

Differential Diagnosis

Differential diagnosis of pigmented fundus lesions of Gardner syndrome includes isolated congenital hypertrophy of retinal pigment epithelium, choroidal nevus, choroidal melanoma, choroidal melanocytoma, hyperplasia of retinal pigment epithelium, and dark subretinal blood.

Prophylaxis

Although no prophylaxis against Gardner syndrome is currently available, routine fundus examination can be helpful for detecting Gardner syndrome in asymptomatic individuals. Routine dilated fundus examination with scleral depression is recommended for all patients with a family history of familial adenomatous polyposis.

Therapy

Management of pigmented fundus lesions in Gardner syndrome is observation. Treatment of intestinal polyps and adenocarcinoma is determined under the care of a gastroenterologist.

Prognosis

Visual prognosis of Gardner syndrome is excellent, as the pigmented fundus lesions of the retinal pigment epithelium are typically asymptomatic. Survival prognosis of Gardner syndrome is determined by the intestinal manifestations of the disease.

Epidemiology

Unclear

Cross-References

▶ Choroidal and/or Ciliary Body and/or Iris Melanoma

- ▶ Congenital Hypertrophy of Retinal Pigment Epithelium
- ▶ Pigmented Lesions of the Conjunctiva
- ▶ Retinal Pigment Epithelium
- ▶ Uveitis, Iridocyclitis

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Gas Tamponade

- ▶ Intraocular Gases

Gass Disease

- ▶ Adult-Onset Foveomacular Vitelliform Dystrophy

Gasserian Ganglion

- ▶ Gasserian Ganglion (Semilunar/Trigeminal Ganglion)
- ▶ Trigeminal Ganglion (Gasserian/Semilunar Ganglion)

Gasserian Ganglion (Semilunar/Trigeminal Ganglion)

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Synonyms

Gasserian ganglion; Semilunar ganglion; Trigeminal ganglion

Definition

Afferent sensory fibers of the trigeminal nerve originate from cell bodies within the *trigeminal ganglion*. A fold of dura, named Meckel cave, houses the sensory trigeminal ganglion also known as the gasserian or semilunar ganglion. Two of the three branches (V1 and V2) of the trigeminal nerve serve solely as sensory nerves whereas the mandibular division (V3) of the trigeminal nerve has both motor and sensory fibers.The sensory root of CN V exits the pons ventrally and fans out to form the

trigeminal ganglion meanwhile the motor fibers of CN V remain separated. Three separate sensory divisions then come off the trigeminal ganglion and continue as the ophthalmic nerve (V1), maxillary nerve (V2), and mandibular nerve (V3).

Cross-References

- ▶ V1 (Ophthalmic Nerve)
- ▶ V2 (Maxillary Nerve)
- ▶ V3 (Mandibular Nerve)

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General: Astigmatism

- ▶ Corneal Astigmatism

Geographic Atrophy

- ▶ Atrophy, Geographic

Geographic Corneal Dystrophy

- ▶ Reis-Bücklers Dystrophy

Geometrical Optics

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Synonyms

Ray optics

Definition

Geometrical optics is a method to describe light propagation by definition of light rays which are perpendicular to wave fronts. A ray is a simplified model of the path of a wave or photon within an optical system which can be calculated by ray tracing using the laws of refraction and reflection. Ray tracing is sufficient for most calculations in ophthalmology and basic optical aberration calculation. Most intraocular lens calculation formulas are based on geometric optical considerations.

Cross-References

- ▶ Law of Reflection: Definition
- ▶ Law of Refraction (Snell's Law)
- ▶ Optical Aberrations
- ▶ Ray Tracing

Gerontoxon

- ▶ Corneal Arcus

Ghost Cell Glaucoma

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Definition

Degenerated red blood cells (ghost cells) cause secondary open-angle glaucoma by blocking the outflow through the trabecular meshwork (Campbell et al. 1976). After a vitreous hemorrhage, red blood cells degenerate (Campbell et al. 1976).

They lose their intracellular hemoglobin and appear as small and tan-colored intraocular bodies with some denatured clumped hemoglobin called *Heinz bodies* (Campbell et al. 1976). The ghost cells migrate into the anterior chamber through a disrupted anterior hyaloid face. Ghost cells are more rigid compared to normal red blood cells, which is a major reason for obstruction of the trabecular meshwork (Campbell et al. 1976; Quigley and Addicks 1980).

Etiology

A disruption in the anterior hyaloid membrane by previous intraocular surgery (e.g., vitrectomy, cataract surgery) or by trauma causes the pathway to the anterior chamber. One to three months after a vitreous hemorrhage, ghost cells appear in the anterior chamber (Montenegro and Simmons 1995).

Clinical Presentation

Intraocular pressure is elevated typically 1–3 months after a vitreous bleeding (Montenegro and Simmons 1995).

Diagnosis

IOP is unilaterally elevated in the eye with previous vitreous hemorrhage. Circulating ghost cells are visible in the anterior chamber. Signs of inflammation like superficial conjunctival injection or intraocular flare are absent. Gonioscopically, ghost cells could be found mainly in the inferior hemicircumference on the trabecular meshwork. Old red blood cells may be found in the vitreous.

Differential Diagnosis

- Uveitis anterior
- Status post-hyphema

Therapy

Local antiglaucomatous therapy should be initiated. Upon failure, irrigation of the anterior chamber, vitrectomy, or trabeculectomy to control IOP are treatment options, which can be discussed with the patient.

Prognosis

Heinz bodies may be washed out over time and ghost cell glaucoma may resolve.

Epidemiology

Ghost cell glaucoma is very rare.

Cross-References

▶ Traumatic Glaucoma

References

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Ghost Image

▶ Monocular Diplopia

Giant Cell Arteritis

▶ Arteritic Ischemic Optic Neuropathy

Giant Papillary (Contact Lens-Induced) Conjunctivitis Disease

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Synonyms

Contact lens-induced conjunctivitis

Definition

Giant papillary conjunctivitis (GPC) An inflammatory response of the superior tarsal conjunctiva to the prolonged presence of a foreign body on the ocular surface.

Etiology

The condition was first observed in contact lens wearers. Ocular prostheses, exposed suture ends, extruded scleral buckles, filtering blebs, corneal foreign bodies, limbal dermoids, and tissue adhesives have also been implicated (Ehlers and Donshik 2008). The condition is most commonly seen in contact lens wearers, particularly patients who wear soft contact lenses (Manzouri et al. 2006). It can occur with hydroxyethyl methacrylate (HEMA) or silicone polymer hydrogel contact lenses. However, it can also occur with rigid contact lenses of either polymethyl metacrylate (PMMA) or gas-permeable polymers (Ehlers and Donshik 2008).

The development of giant papillary conjunctivitis is attributed to a combination of mechanical irritation of the superior limbus and a hypersensitivity reaction to material adherent to the contact lenses, sutures, or ocular prostheses (Dunn and Heidemann 2011). A study on Rhesus monkeys demonstrated that coated contact lenses lead to cellular infiltration of the conjunctiva with eosinophils and plasma cells. This reaction was not noted in virgin contact lenses or lenses from non-GPC contact lens wearers. Additionally, the tears of patients with active GPC have been found to have elevated levels of immunoglobulin and various cytokine levels. These findings suggest that there may be an antigen on coated contact lenses contributing to the immune reaction in GP-C. The presence of neutrophil chemotactic factor released from injured conjunctival cells supports the theory that a mechanical cause may also be involved (Ehlers and Donshik 2008). Minimizing the build-up of lens deposits appears to reduce the chance of developing mechanical and immunologic stimuli for the condition. The frequency of contact lens replacement is a significant variable in the development of giant papillary conjunctivitis. Individuals on a 1-day to 3-week replacement cycle were less likely to develop this condition than individuals on a longer replacement schedule (Dunn and Heidemann 2011).

In some cases, giant papillary conjunctivitis appears to be related to thimerosal exposure. Lens care solutions used in most reported cases contained thimerosal. However, only a minority of patients exhibited reactions to thimerosal on patch testing. The incidence of giant papillary conjunctivitis is decreasing as most contact lens solutions no longer contain thimerosal. Hypoxia of the epithelium beneath the lens may be associated, which would be expected to be most significant beneath the superior lid (Arffa 1997).

Clinical Presentation

Giant papillary conjunctivitis may present as early as 3 weeks to 8 months after the start of soft contact lens use and 14 months to 8 years after the start of hard contact lens use (Dunn and Heidemann 2011). Classic symptoms of GPC include decreased contact lens tolerance, increased mucus production, and excessive contact lens displacement, usually superiorly (Ehlers and Donshik 2008). Early symptoms of giant papillary conjunctivitis include inner canthus mucus discharge in the morning and itching upon removal of the contact lenses. During the early stages of the disease, the conjunctiva may appear normal. The symptoms become more marked as

the disease progresses. The patient may begin to experience a foreign body sensation, conjunctival injection, photophobia, tearing, and crusting. Blurry vision may also be a symptom of the disease secondary to mucus coating of the lens and increased lens mobility and instability. During this stage of the disease, the superior tarsal conjunctiva becomes thickened and hyperemic. Small papillae develop initially, which progress in size and number over time to become giant papillae (Manzouri et al. 2006).

The papillae of giant papillary conjunctivitis are defined as greater than 0.3 mm in diameter. Giant papillae are defined as being greater than 1.0 mm in diameter (Dunn and Heidemann 2011). The distribution of the giant papillae varies depending upon the type of lens worn. Soft contact lens wearers develop papillae along the superior edge of the tarsal plate initially and progress to involve the entire central area of the tarsal conjunctiva. Hard contact lenses tend to be smaller, and wearers of these lenses develop papillae closer to the margin of the superior lid (Manzouri et al. 2006). These papillae tend to be fewer in number with a crater-like or flattened appearance (Dunn and Heidemann 2011). Ocular prostheses tend to cause a generalized papillary reaction. Filtering blebs and exposed sutures cause a more localized GPC, usually centered around the bleb or exposed suture (Ehlers and Donshik 2008). Subepithelial opacities are often present, and a pannus may be noted beneath the abnormal epithelium (Arffa 1997). The bulbar conjunctiva and the inferior fornix usually appear normal. In the advanced stages of the disease, patients may become increasingly intolerant of their contact lenses (Manzouri et al. 2006).

Diagnosis

A history of contact lens use with details of contact lens age, type, and frequency of replacement should be taken. For diagnosis, slit-lamp examination of the superior tarsal conjunctiva by eversion of the upper lids reveals hyperemia and injection of the upper tarsal conjunctiva, making the vascular arcade difficult to discern. Additionally, large papillae greater than 0.3 mm can be visualized on the superior tarsal conjunctiva (Ehlers and Donshik 2008). Fluorescein staining of the superior corneal epithelium of the papillae may be punctate, extending from the limbus in a V pattern toward the visual axis (Arffa 1997).

Differential Diagnosis

Differential diagnosis includes vernal keratoconjunctivitis. Contact lens history and patient age may be helpful in distinguishing these conditions as vernal keratoconjunctivitis is uncommon after the early twenties (Manzouri et al. 2006). Additionally, patients with vernal keratoconjunctivitis frequently have a history of allergic rhinitis, atopic dermatitis, and asthma (Dunn and Heidemann 2011).

Prophylaxis

The development of giant papillary conjunctivitis can be reduced by meticulous contact lens hygiene, and frequent replacement of lenses to minimize lens surface deposits (Dunn and Heidemann 2011).

Therapy

The goal of therapy in giant papillary conjunctivitis is resolution of the burning, itching, and excess mucus production that characterize the condition. Reduction or cessation of contact lens use for 2–4 weeks is the primary treatment for giant papillary conjunctivitis (Ehlers and Donshik 2008). After resolution of the signs and symptoms of GPC, lens wear can be reinstituted by refitting, switching to alternate better tolerated lenses, or avoiding solutions containing thimerosal (Arffa 1997). Studies have shown that changing to a different contact lens polymer allows over 80% of GPC patients to continue contact lens wear (Ehlers and Donshik 2008). For patients who may be significantly handicapped by the

discontinuation of contact lens use, including individuals with keratoconus or anisometropia, modification of their contact lens care routine and wear schedule may help to relieve many of the symptoms of giant papillary conjunctivitis. Because of the well-established relationship between lens deposits and giant papillary conjunctivitis, the use of daily disposable soft contact lenses or frequent replacement contact lenses is the best solution. Individuals for whom this may be cost-prohibitive or who require specialty lenses or rigid-gas permeable lenses should adopt a daily lens care regime, including use of a surfactant cleaner and "rub" routine. Disinfection of the lenses with hydrogen peroxide is the least likely method to further traumatize the conjunctiva (Dunn and Heidemann 2011).

When discontinuation of contact lens wear and refitting with frequent replacement contact lenses is unsuccessful, the conjunctival inflammation may be managed pharmacologically with the goal of reducing histamine release and local inflammation (Ehlers and Donshik 2008). Topical mast cell stabilizers, such as cromolyn sodium, have been shown to be effective in resolution of early giant papillary conjunctivitis when combined with lens hygiene. This class of medications stabilizes the mast cell membrane and inhibits type I hypersensitivity reactions. Cromolyn sodium can be applied with continued contact lens use. If the condition does not improve, discontinuation of contact lens wear may be necessary with gradual reintroduction after resolution of symptoms. Nonsteroidal anti-inflammatory drugs (NSAIDs), such as suprofen, have been shown to reduce papillae and symptoms associated with the condition. NSAIDs appear to work by inhibiting mast-cell stimulated prostaglandin biosynthesis. Treatment with topical corticosteroids can be beneficial in the acute phase of giant papillary conjunctivitis to reduce tarsal hyperemia and inflammation. The need for corticosteroids is an indication of severity of disease, and contact lens use should be discontinued until corticosteroids are no longer necessary (Dunn and Heidemann 2011). If corneal epithelial changes do not resolve with discontinuation of lens wear, surgical treatment options may be necessary. In some cases, limbal or conjunctival autografts have successfully restored the corneal surface (Arfa 1997).

Prognosis

If contact lens wear is discontinued, the prognosis is good, and the disease may resolve within a few weeks to several months. Early recognition and treatment of the condition is important for ensuring contact lens comfort and the individuals continued ability to wear contact lenses (Dunn and Heidemann 2011). If left untreated, the disease continues to progress. The epithelium thickens, becomes grayer, and involves an increasingly greater area of the conjunctiva. The pannus progresses centrally and vascularization of the deep stroma may develop. Superficial stromal scarring may also be present and recurrent ulceration can occur (Arffa 1997).

Epidemiology

An estimated 1–5% of soft contact lens wearers and 1% of hard contact lens wearers have clinically significant signs and symptoms of giant papillary conjunctivitis. The incidence of giant papillary conjunctivitis is generally considered to be higher amongst extended wear contact lens users compared to daily wear soft lens wearers. The syndrome can occur at any age and is seen with equal frequency between males and females (Dunn and Heidemann 2011).

Cross-References

▶ Vernal Conjunctivitis/Keratoconjunctivitis

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Glands of Krause, Glands of Moll, Glands of Wolfring, Glands of Zeis

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Synonyms

Accessory lacrimal glands; Apocrine or sweat glands of the eyelid; Sebaceous glands of the eyelid

Definition

Glands of Krause

Exocrine and aqueous secreting accessory lacrimal glands located in the lamina propria of the conjunctival fornices (superior > inferior).

Glands of Wolfring

Exocrine and aqueous secreting accessory lacrimal glands located above the superior border of the upper lid tarsus.

Glands of Moll

Specialized apocrine sweat glands located at the base of the lashes anterior to the Meibomian glands.

Glands of Zeis

Modified sebaceous holocrine glands located at the base of eyelash follicles.

Structure

Glands of Krause and Wolfring possess a histologic structure similar to the lacrimal gland.

Glands of Moll are tubular, large apocrine gland.

Glands of Zeis are unilobular sebaceous gland units associated with follicles.

Function

The eyelid glands produce the tear film which nourishes, lubricates, and protects the ocular surface.

- Glands of Krause and Wolfring are responsible for aqueous tear secretion.
- Glands of Moll and Zeis secrete part of the lipid component of the tear film. Moll's secretions have been found to have bacteriolytic properties as well and may play a role in local immune defense.

Clinical Relevance

Abnormal functioning of any of the glands may lead to dry eye conditions. Cysts and carcinomas of these glands may occur.

- Glands of Krause and Wolfring are affected in Sjogren syndrome and graft-versus-host disease.
- Glands of Moll can develop ductal cysts, including apocrine hidrocystomas (smooth cysts arising from the glands of Moll); they can also develop apocrine carcinoma.
- Glands of Zeis can develop an acute infection of the sebaceous material within these glands resulting in an external hordeolum; sebaceous carcinoma may arise in these glands.

Cross-References

- ▶ Accessory Lacrimal Glands
- ▶ Dry Eye
- ▶ Graft-Versus-Host Disease: Overview
- ▶ Hidrocystoma, Apocrine
- ▶ Hordeolum
- ▶ Sebaceous Carcinoma
- ▶ Sweat Glands of Eyelid
- ▶ Tear Film (Tears)

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Glare Testing

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Synonyms

Disability glare testing

Definition

Methods of psychophysical quantification of the effects of ▶ glare on visual function. In clinical use, "glare testing" is synonymous with measuring the effects of straylight-induced effects on visual function. Typically, a ▶ contrast sensitivity test is repeated after introducing glare by a defined glare source. The difference between the measurement without and with glare denotes the glare effect, also referred to as glare sensitivity or disability glare. There are multiple chart-based tests or view-in devices in use. The C-Quant™ (Oculus Optikgeräte) is the most basic method for the psychophysical quantification of straylight effects.

Questionnaires for the psychometric quantification of glare-induced subjective disturbances and devices for adaptometry also measure glare effects but are generally not considered glare tests.

Cross-References

- ▶ Glare, General

Glare, General

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Synonyms

Disability glare

Definition

A subjective disturbance of vision induced by too high luminances or luminance differences across the visual field. A reduction of visual functions due to glare is common (disability glare) but not a necessary feature of glare.

Basic Characteristics

There are different types of glare: (1) *adaptation glare* due to (momentary) mis-adaption to the actual luminance, e.g., changing from a dark to a brightly lit room after dark adaptation; (2) *absolute glare*, if no adaptation is possible, e.g., glare by sunlight; and (3) *simultaneous glare*, if luminances are distributed inequally within visual field and straylight causes a contrast reduction

(veiling) of the retinal image. The latter form is the clinically most important form of glare and often meant if clinicians refer to "glare." A glare source of defined luminance and size acts at a certain glare angle. The glare source can either be the light source itself (e.g., the sun, headlights) or objects that reflect the light of a light source (e.g., a newspaper that reflects bright light).

Cross-References

▶ Glare Testing

Glaucoma Associated with Pigment Dispersion Syndrome (PDS)

▶ Pigmentary Glaucoma

Glaucomatocyclitic Crisis

▶ Posner-Schlossman Syndrome

Globe, Displacement of, in Orbital Disorders

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Synonyms

Proptosis (for forward displacement of the globe)

Definition

Displacement of the globe from its normal anatomical location due to various orbital processes.

Etiology and Occurrence

Globe displacement may result from a wide variety of neoplastic, inflammatory, infectious, traumatic, and vascular conditions. Any mass lesion of the orbit may cause proptosis or displacement of the eye including primary tumors such as lacrimal epithelial tumors (pleomorphic adenoma, adenoid cystic carcinoma), mesenchymal tumors (fibrous histiocytoma, rhabdomyosarcoma), and neurogenic tumors (sphenoid wing meningioma, optic nerve glioma, neurofibroma, schwannoma). In addition, metastatic lesions, representing 2–3% of all orbital tumors, are usually characterized by a rapid onset of orbital symptoms including globe displacement. The most common primary sites of metastatic carcinoma to the orbit are the breast, lung, prostate, gastrointestinal tract, and kidney.

Lymphoproliferative diseases are uncommon in the orbit and account for 5% of all orbital mass lesions. Lymphoid lesions include lymphoproliferative reactive and atypical diseases and lymphomas. Malignant orbital lymphomas are usually located in the anterior orbit and may mold to the globe and adjacent structures.

Inflammatory diseases are the most common orbital lesions which can cause globe displacement. Most notably Graves' disease, which accounts for 50% of all orbital lesions, causes exophthalmos or forward displacement of the globe. Other inflammatory causes include idiopathic orbital inflammation (pseudotumor), myositis, and Wegener's granulomatosis.

Other causes of globe displacement include infectious processes (orbital cellulitis), trauma (orbital fractures), and structural disorders (dermoid cysts, mucoceles). In addition, vascular lesions are an important cause of globe displacement including capillary hemangioma, cavernous hemangioma, lymphangioma, and arteriovenous fistula.

Classification

The direction of globe displacement may carry diagnostic significance and can be classified by the following locations:

- Inferior displacement: fibrous dysplasia, frontal mucocele, lymphoma, neuroblastoma, neurofibroma, schwannoma, subperiosteal hematoma, thyroid orbitopathy
- Superior displacement: lacrimal sac tumors, lymphoma, maxillary sinus tumors, metastatic tumors
- Lateral displacement: ethmoid mucocele, lacrimal sac tumors, metastatic tumors, nasopharyngeal tumors, rhabdomyosarcoma
- Medial displacement: lacrimal fossa tumors, sphenoid wing meningioma

Diagnostics

A complete medical and ophthalmic history including time course of the disease, past trauma, and systemic illnesses should be elicited. A careful and complete ophthalmic exam including external and periorbital inspection for lid findings (edema, ptosis, retraction) and assessment for a palpable mass should be completed. Hertel exophthalmometry should be done to measure the degree of anterior displacement, and motility should be assessed. Imaging by computed tomography or magnetic resonance imaging is almost always indicated.

Cross-References

- ▶ Accessory Lacrimal Glands
- ▶ Orbit, Inflammation of
- ▶ Proptosis
- ▶ Trauma, Lacrimal Sac and Nasolacrimal Duct

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Glomangioma

▶ Vascular Tumors Disease of the Conjunctiva

Glucocorticoids

▶ Corticosteroids, Use in Ophthalmology

Glue

▶ Tissue Adhesives, Cyanoacrylate, for Anterior Segment

GM2 Gangliosidoses

▶ Tay-Sachs Disease (GM2 Gangliosidosis Type I)

Goblet Cells, Mucin Tear Secretion by

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Synonyms

Mucus-secreting cells

Definition

Cells recognized as a source of mucus for the tear-film complex.

Structure

Conjunctival goblet cells appear in histological sections as oval-shaped cells containing rich amounts of intracytoplasmic mucus (Doughty 2012). Cytoplasmic staining is characteristically periodic acid-Schiff (PAS) positive, reflecting the high density of glycosylated glycoproteins within these cells (Doughty 2012). Goblet cell location

varies depending on their degree of maturation with more mature cells residing near the apical surface of the conjunctival epithelium; the distribution of goblet cells is related to differences in exposure, with cell numbers being higher in the superior and inferior bulbar conjunctiva compared to the interpalpebral conjunctiva (Doughty 2012).

Function

Goblet cells comprise the main source of mucus secreted into the tear-film complex (Inatomi et al. 1996; Doughty 2012; Gipson 2004). Mucus secretion is influenced by environmental and autonomic factors (Plugfelder 2011). A gel-forming mucin, MUC5AC, secreted by conjunctival goblet cells assists in the maintenance of a moist and lubricated ocular surface (Inatomi et al. 1996). Secreted mucins are negatively charged and move freely over similarly negatively charged membrane-associated mucins of the conjunctival and corneal epithelium also known as *glycocalyx* (Gipson 2004). It is believed that repellent forces between these two mucin layers promote debris removal from the surface epithelium, hence their recognition as an integral component of the lacrimal function unit (Plugfelder 2011).

Clinical Relevance

Ocular surface diseases are associated with drying, increased deposition of keratin in the conjunctival epithelium, reduced goblet cell density, and reduced secretion of gel-forming mucins (Plugfelder 2011; Doughty 2012). A broad group of entities are associated with impaired goblet cell function. These include tear-film dysfunction, Stevens-Johnson syndrome, and ocular cicatricial pemphigoid (Sangwan and Tseng 2001).

Cross-References

► Tear Film (Tears)

References

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Goldenhar Syndrome

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Synonyms

Facio-auriculo-vertebral spectrum; First and second branchial arch syndrome; Oculo-auriculo-vertebral spectrum

Definition

Congenital syndrome of the first and second brachial arches that includes malformations of the eyes, ears, mandible, and cervical spine.

Etiology

Because there has been no agreement on the minimal diagnostic criteria, Goldenhar syndrome may be more appropriately termed oculo-auriculo-vertebral spectrum (OAVS). This nomenclature emphasizes the continuum of ocular, auricular, and vertebral anomalies also referred to as hemifacial microsomia, facio-auriculo-vertebral

syndrome, otomandibular dysostosis, Goldenhar syndrome, or first and second branchial arch anomalies.

In most cases, OAVS appears to occur sporadically; however, family histories suggest an autosomal dominant or recessive inheritance in several documented cases. Possible loci have been suggested at 14q22 and 5p15.33-pter. Mutations in the SALL1 gene at 16q12.1 can result in an OAVS phenotype (Tasse et al. 2007). In addition, some researchers suggest that this condition may result from a somatic mutation or disruption during embryogenesis which interferes with the development of the first two brachial arches. Also, there has been speculation of its association with maternal diabetes and with thalidomide or retinoic acid intake during pregnancy. The teratogen thalidomide appears to result in OAVS anomalies particularly when the drug is ingested during weeks 6–8 of gestation (Gorlin et al. 1990).

Clinical Presentation

Patients with the OAV spectrum have unilateral or bilateral hemifacial microsomia, including decreased jaw and cheek growth, microtia, pretragal skin tags or blind fistulas, hearing loss, and facial weakness. Patients may also have vertebral, neurologic, cardiovascular, and genitourinary abnormalities, in addition to characteristic ophthalmic abnormalities (Alecksic et al. 1975).

Ocular manifestations include epibulbar dermoid (78%), lipodermoid (47%), upper eyelid coloboma (24%), Duane syndrome, and, less commonly, corneal hypoesthesia, microcornea, microphthalmia, anophthalmia, ocular coloboma, iris atrophy, and anterior polar cataract. An absent, abnormal, or ectopic caruncle may predict nasal involvement and help to make a diagnosis of OAVS (Spierer and Wygnanski-Jaffe 2011).

Epibulbar dermoids (Fig. 1) usually occur in the inferotemporal quadrant, straddling the limbus, and are covered by conjunctiva. They are mixed tissue choristomas and can have hair shafts protruding from the surface. They occur bilaterally in 25% of patients. These dermoids can cause amblyopia either by direct obstruction of the visual axis or, more commonly, by anisometropic amblyopia resulting from induced astigmatism (Baum and Feingold 1973).

Goldenhar Syndrome, Fig. 1 Photograph of an inferotemporal, limbal epibulbar dermoid (Courtesy of Dr. Alex V. Levin, Wills Eye Institute)

Lipodermoids are reported less frequently, occurring either alone or in association with an epibulbar dermoid. They are most commonly located over the lateral rectus muscle or in the superotemporal quadrant, do not invade the cornea, and are often bilateral. They may infiltrate extraocular muscles and restrict eye movement (Baum and Feingold 1973).

Diagnostics

The minimum criteria for the clinical diagnosis of OAVS are the presence of at least two of the following: otic hypoplasia, hemifacial microsomia, lateral facial cleft, epibulbar dermoid and/or upper eyelid coloboma, and vertebral anomalies.

Differential Diagnosis

Treacher Collins-Franceschetti syndrome
Pierre Robin syndrome
Hemifacial microsomia
Cervico-oculo-acoustic syndrome
Townes-Brocks syndrome
Microtia-anotia syndrome
Aplasia cutis with epidermal dermoids

Oculo-auriculo-frontonasal syndrome
Goltz syndrome

Prophylaxis

Prenatal ultrasound may identify facial and ocular anomalies.

Therapy

Amblyopia should be treated appropriately. Surgical excision, usually via superficial keratectomy, is indicated for epibulbar dermoid tumors that exhibit continued growth, ocular irritation, amblyopia unresponsive to glasses and occlusion, or unacceptable cosmesis. Oculoplastic repair of upper eyelid colobomas are usually performed after the first year of life. Although lipodermoid may represent a cosmetic concern, surgery is often difficult, and it is best to restrict excision to the surface of the mass.

Prognosis

Individuals typically have a normal life span and normal intelligence.

Epidemiology

Incidence estimated to be 1 in 5,600 births.

Cross-References

- ▶ Choristomas
- ▶ Limbal Dermoid
- ▶ Nutritional Amblyopia
- ▶ Treacher Collins-Franceschetti Syndrome (Mandibulofacial Dysostosis)

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Gonococcal Conjunctivitis

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Definition

Inflammation of the conjunctiva caused by *Neisseria gonorrhoeae* infection.

Etiology

Gonococcal conjunctivitis may be acquired through direct genital-eye transmission, genital-hand-eye contact, or maternal-neonate transmission during vaginal delivery.

Clinical Presentation

Gonococcal conjunctivitis is characterized by hyperacute onset of purulent exudates, conjunctival chemosis and hyperemia, and eyelid swelling. It may also be associated with the formation of membranes and preauricular lymphadenopathy. Keratitis is the most frequent cause of sight-threatening complication and occurs in 15–40% of cases.

Notable signs of corneal involvement include marginal infiltrates, epithelial haze, epithelial defects, and peripheral infectious keratitis. If left untreated, keratitis may progress to ulceration and eventually perforation.

In neonates, symptoms are typically bilateral and begin within 2–5 days after parturition.

Diagnosis

In cases of neonatal gonococcal conjunctivitis, a prenatal history is vital and cervical specimens should be taken from the mother for culture. A full ocular and general physical exam should be performed to diagnose and assess the extent of disease.

Conjunctival scrapings submitted for Gram and Giemsa staining should reveal intracellular gram-negative diplococci present inside neutrophils.

Conjunctival swabs should also be planted on chocolate agar in a CO_2-enriched atmosphere or Thayer-Martin media.

Differential Diagnosis

Differential diagnosis includes chemical conjunctivitis, chlamydial and other nongonococcal bacterial conjunctivitis, and herpetic conjunctivitis.

Prophylaxis

Prophylactic recommendations include tetracycline (1%) drops and erythromycin (0.5%) ointment. Silver nitrate drops are used less commonly as they may cause chemical conjunctivitis and do not provide prophylaxis against chlamydia.

Therapy

The mainstay of treatment of gonococcal disease is systemic antibiotics. Due to increasing prevalence of penicillin-resistant *N. gonorrhoeae*, ceftriaxone is prescribed as first-line treatment. Gonococcal conjunctivitis without ulceration may be treated with a one-time, intramuscular dose of ceftriaxone (1 g). Patients with corneal ulceration should be admitted to the hospital and treated with intravenous ceftriaxone (1 g IV every 12 h) for 3 days. Patients with a penicillin allergy may be treated with spectinomycin (2 g IM) or ciprofloxacin (500 mg bid for 5 days).

Non-disseminated neonatal conjunctivitis is treated with a single intravenous or intramuscular ceftriaxone (25–50 mg/kg or up to 125 mg). Alternatively, cefotaxime may be prescribed as an intramuscular or intravenous injection (100 mg/kg). In disseminated infections, hourly saline irrigation of the conjunctiva may be initiated to clear discharge. If clinical signs of corneal involvement are present, topical erythromycin or gentamicin ointment or a topical flouroquinolone should be considered. Patients should also be treated for chlamydia with systemic erythromycin (12.5 mg/kg oral or IV qid for 14 days) as coinfection can occur and systemic involvement, such as pneumonitis and otitis media, can lead to significant morbidity.

Prognosis

Prognosis is excellent if treatment is started while infection is localized. Visual prognosis may be limited in patients with significant corneal involvement with subsequent scarring and/or perforation.

Disseminated gonococcal infection with meningitis, pneumonia, and sepsis resulting in death is a rare complication in neonates.

Epidemiology

The incidence of neonatal gonococcal conjunctivitis is estimated at approximately 100 per 100,000 in the United States.

Non-neonatal infections are most common in adolescents and young adults.

Cross-References

► Conjunctivitis

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Good Acuity Plus Photophobia

► Transient Light-Sensitivity Syndrome

Gorlin Syndrome

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Synonyms

Basal cell nevus syndrome; Nevoid basal cell carcinoma syndrome

Definition

A rare autosomal dominant disorder characterized by multiple nevoid basal cell carcinomas early in life. It is a multisystemic disease involving multiple organ systems (American Academy of Ophthalmology 2006–2007; Albert and Jakobiec 2008).

Etiology

Tumors are indistinguishable from noninherited forms of basal cell carcinoma, arising from the basal cell layer of the epithelium. The gene though to be responsible for Gorlin syndrome is the patched gene (PTCH), found on 9q22.3-q31. It is thought to be a tumor suppressor with one germline defect in affected families. Complete penetrance with variable expressivity is observed (Gorlin 1995; Bale 1997; Shields and Shields 1999; American Academy of Ophthalmology 2006–2007; Albert and Jakobiec 2008).

Clinical Presentation

Gorlin syndrome may present with multiple basal cell carcinomas at a young age. Eyelid basal cell carcinomas occur in 25% of cases and are indistinguishable from noninherited forms of basal cell carcinoma.

Other ophthalmic findings in Gorlin syndrome include congenital cataracts, orbital cysts, hypertelorism, colobomas, and medullated nerve fiber layer of the retina. Other features include mandibular cysts, macrocephaly, frontal bossing, polydactyly, palmar or plantar pits, and medulloblastoma (Gorlin 1995; Bale 1997; Shields and Shields 1999; American Academy of Ophthalmology 2006–2007; Albert and Jakobiec 2008).

Diagnostics

Excisional biopsies of suspect lesions are histologically indistinguishable from basal cell carcinoma. Imaging is necessary when clinically correlated, including MRI of the brain, dental radiography, and a skeletal survey (Gorlin 1995; Bale 1997; Shields and Shields 1999; American Academy of Ophthalmology 2006–2007; Albert and Jakobiec 2008).

Differential Diagnosis

Xeroderma Pigmentosa

Prophylaxis

Patients with Gorlin syndrome may be extremely susceptible to ionizing radiation and sun exposure. Patient should be counseled to avoid sun exposure (Gorlin 1995; Bale 1997; Shields and Shields 1999; American Academy of Ophthalmology 2006–2007; Albert and Jakobiec 2008).

Therapy

Surgical excision is recommended for a patient with a limited number of lesions. Topical 5-fluorouracil with or without topical tretinoin may be useful for patients with extensive lesions. Oral isotretinoin may be an option for patients who are at high risk for developing many additional lesions.

Prognosis

Patients may have multiorgan involvement and will need care by appropriate specialists, including dermatologists, dentists, oncologists, cardiologists, and orthopedic surgeons.

Epidemiology

Incidence is rare and occurring in about 1 per 50,000–150,000 people and in 0.7% of patients with basal cell carcinoma. Fair skinned patients with substantial sun exposure may be more susceptible (Shields and Shields 1999; American Academy of Ophthalmology 2006–2007; Albert and Jakobiec 2008).

Cross-References

- ▶ Basal Cell Carcinoma of Eyelid
- ▶ Basal Cell Nevus Syndrome (Gorlin Syndrome)

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Gradenigo Syndrome

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Synonyms

Gradenigo-Lannois syndrome; Petrous apicitis

Definition

Gradenigo syndrome is a rare but sometimes serious infectious/inflammatory syndrome, associated with localized inflammation at the apex of the petrous temporal bone, a location in which the trigeminal (CN V) nerve is closely related to abducens nerve (CN VI) and facial (CN VII) and vestibulocochlear (CN VIII) nerves.

Etiology

Causes include inflammation (e.g., petrositis secondary to otitis and mastoiditis), infection typically due to aerobic microorganisms, extradural abscess, tumors (e.g., cholesteatoma, chordoma, meningioma, nasopharyngeal carcinoma, metastatic disease), and skull base fracture.

Clinical Presentation

Gradenigo syndrome is characterized by a clinical triad: retro-orbital pain in the distribution of the ophthalmic division of trigeminal nerve (CN V), diplopia due to abducens nerve (CN VI) palsy, and otorrhea due to suppurative otitis media. Facial (CN VII) palsy and deafness, due to compromise of vestibulocochlear nerve (CN VIII), also may manifest as components of the syndrome.

History

It was first described by Giuseppe Gradenigo in 1904, as a serious complication of otitis media. In the postantibiotic era, infection is a much less common cause of the syndrome.

Diagnosis

The diagnosis of Gradenigo syndrome is a clinical diagnosis supported by either computed tomography (CT) or magnetic resonance imaging (MRI) findings.

Differential Diagnosis

The differential diagnosis of Gradenigo syndrome includes Ramsay Hunt syndrome (geniculate Herpes Zoster), neoplastic disorders involving petrous bone, and closed head trauma.

Therapy

High-dose antibiotic treatments, both systemic and topical, are recommended for infectious etiologies. Treatment, in severe cases failing maximum medical therapy, may also require more aggressive and radical surgical intervention (e.g., apical petrosectomy) to debulk the infection.

Prognosis

Earlier diagnosis and treatment may limit disease progression and more severe and potentially life-threatening complications.

Epidemiology

The incidence of infectious Gradenigo syndrome in the United States has been reduced by earlier diagnosis and treatment with broad-spectrum antibiotics but may still be as high as 2 per 100,000 individuals with acute otitis media. Gradenigo syndrome however remains a problem in lesser-developed countries.

Cross-References

- ▶ Facial Nerve Palsy
- ▶ Sixth Nerve Palsy

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Gradenigo-Lannois Syndrome

► Gradenigo Syndrome

Graft-Versus-Host Disease: Overview

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Definition

Graft-versus-host disease (GVHD) is a major complication from allogeneic hematological stem cell transplantation. It is a systemic inflammatory condition due to attack of host tissue by immunocompetent cells from the donor (Albert et al. 2008).

Etiology

GVHD is the recognition of allogeneic differences and destruction of host peptides by immune cells of the donor. Activation of donor immune cells leads to secretion of IL-2, resulting in clonal expansion and proliferation of T lymphocytes (Albert et al. 2008).

Acute GVHD is due to conditioning regimen (radiation and/or chemotherapy) that damages host tissue (Albert et al. 2008). This leads to production of pro-inflammatory cytokines such as IL-1 and TNF-α that increase expression of human leukocyte antigen (HLA) alloantigens and adhesion molecules on the surface of host cells, activating donor type 1 helper T cell (Albert et al. 2008).

Chronic GVHD is predominantly a type 2 helper T cell response with lymphoproliferation, increased IgE synthesis, and production of IL-4 and IL-10 (Albert et al. 2008). In contrast to acute GVHD, donor antigen-presenting cells are also involved in the pathogenesis (Albert et al. 2008).

Clinical Presentation

Acute GVHD develops within 100 days of transplantation and chronic GVHD develops after day 100 (Albert et al. 2008). Ocular GVHD can affect all layers of the eye including the lid, meibomian gland, vitreous, and choroid, but it mainly affects ocular surface and lacrimal gland (Hasanain et al. 2013). Acute ocular GVHD often presents with conjunctival hyperemia, chemosis, and pseudomembrane formation (Hasanain et al. 2013). Chronic GVHD often presents with keratoconjunctivitis sicca along with chronic blepharitis and meibomian gland dysfunction (Hasanain et al. 2013). Sterile conjunctivitis, cicatricial lagophthalmos, and retinal microvascular occlusive disease are also commonly observed (Hessen and Akpek 2012).

Diagnosis

Acute ocular GVHD is diagnosed by clinical presentation. Diagnosis of chronic ocular GVHD needs to be confirmed by (1) biopsy or Schirmer test and (2) involvement of at least one other organ (Hasanain et al. 2013).

Differential Diagnosis

Infection, total body irradiation, ocular toxicity of chemotherapy, immunosuppressive therapy, meibomian gland dysfunction, and keratoconjunctivitis sicca are due to other causes.

Prophylaxis

One major prophylaxis method is optimal HLA-matching between donor and recipient. Donor T cell depletion through alemtuzumab (anti-CD52) and anti-thymocyte globulin can also prevent GVHD, but this increases the rate of graft failure, relapse of malignancy, infections, and Epstein-Barr virus-associated lymphoproliferative disorder (Hasanain et al. 2013). Pharmacologic agents that can be used are the combined use of calcineurin inhibitors with low doses of methotrexate (Hasanain et al. 2013). Reduced intensity conditioning regimens reduce tissue damage and thus lower intensity of cytokine storm (Hasanain et al. 2013).

Therapy

Treatment options for ocular GVHD include lubrication with artificial non-preserved phosphate-free tears (Hessen and Akpek 2012); tear preservation with punctal occlusion (silicone plugs or thermal cauterization) (Hessen and Akpek 2012); reduction of inflammation with short-term, low-frequency application of topical steroids and long-term control with topical cyclosporine eye drops (Hessen and Akpek 2012); prevention of tear evaporation with warm compresses and ointments such as erythromycin (Hessen and Akpek 2012); epithelial support with autologous serum eye drops, contact lenses (bandage soft contact lenses, scleral lenses, or prosthetic replacement of ocular surface ecosystem), or sutureless amniotic membrane; and surgery for severe cases of ocular surface disruption (Hessen and Akpek 2012).

Prognosis

Mortality due directly or indirectly to acute GVHD may reach 50% (Albert et al. 2008). Acute GVHD leading directly to chronic GVHD has the worse prognosis compared to chronic GVHD with a remission period after acute GVHD and de novo chronic GVHD (Hasanain et al. 2013). Presence of pseudomembranous conjunctivitis is associated with poor prognosis (Hasanain et al. 2013).

Epidemiology

Acute and chronic GVHD develops in approximately 40% and 30–70%, respectively, in HLA-matched patients (Hessen and Akpek 2012). Ocular manifestations occur in 60–90% of patients with chronic GVHD but are uncommon in acute GVHD (Hessen and Akpek 2012).

Cross-References

- ▶ Blepharitis
- ▶ Conjunctivitis
- ▶ Keratoconjunctivitis: Overview
- ▶ Lagophthalmos
- ▶ Meibomian Gland Dysfunction
- ▶ Thermal Cautery

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Gram-Negative Bacteria

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Definition

A group of microorganisms that will not retain a crystal violet stain on gram staining method.

Structure

As opposed to gram-positive bacteria, gram-negative bacteria maintain the cell wall shape by a thin layer of peptidoglycan that is surrounded by an outer membrane. The outer membrane provides an important role in the protection from host environment, and it is linked to the peptidoglycan through lipoproteins. Lipid A is a component of the outer membrane which acts as a strong activator of the innate immune system. Few kinds of proteins that are found on the outer membrane play a role in the virulence of these organisms. Periplasmic space is an area that is found between the inner and outer membranes that many enzymatic processes will take place at. Other structures which could also be found in the gram-positive bacteria include capsule which is useful in the protection from phagocytosis, pili that are used by bacteria for adherence or sexual reproduction and flagellum for movement.

Function

Certain types of bacteria are found in the normal flora of human bodies. In the ocular flora, gram-negative bacteria that could be isolated include *Haemophilus* species, *Neisseria* species, and *Pseudomonas* species. Recent studies suggested that normal flora could help minimize the inflammations, act as a barrier against harmful pathogens, maintain the immune system, inhibit the apoptosis, and accelerate the wound repair.

Clinical Relevance

Many ocular infections have been related to gram-negative bacteria. These infections could involve any part of the eye and vary in their course and treatment. Keratitis, dacryocystitis, cellulitis, conjunctivitis, corneal ulcer infections, and endophthalmitis are examples of ocular diseases that could be a result of gram-negative bacterial pathology.

Cross-References

▶ Gram-Positive Bacteria

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Gram-Positive Bacteria

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Definition

A group of microorganisms that will stain crystal violet on gram staining method.

Structure

The main theme for the gram-positive bacteria is a thick layer of peptidoglycan that will provide protection and maintain the cell wall shape and structure. Additionally, few bacteria have lipoteichoic acid and teichoic acid in their walls. The main functions of teichoic acid are to further strengthen the cell wall, help in the sequestration of calcium ion, and act as an activator of innate immune system. Other structures which could be found regardless of the bacteria gram stain include capsule which is useful in the protection from phagocytosis, pili that are used by bacteria for adherence or sexual reproduction and flagellum for movement.

Function

Certain types of bacteria are found in the normal flora of human bodies. In the ocular flora, gram-positive bacteria that could be isolated include *Staphylococci*, *Corynebacterium*, *Streptococcus* species, and *Propionibacterium* species. Recent studies showed that this flora could help minimize the inflammations, act as a barrier against harmful pathogens, maintain the immune system, inhibit the apoptosis, and accelerate the wound repair.

Clinical Relevance

Many ocular infections have been related to gram-positive bacteria. These infections could involve any part of the eye and vary in their course and treatment. Hordeolum, blepharitis, keratitis, dacryocystitis, cellulitis, conjunctivitis, corneal ulcer infections, and endophthalmitis are examples of ocular diseases that could be a result of gram-positive bacterial pathology.

Cross-References

► Gram-Negative Bacteria

Further Reading

Deibel JP, Cowling K (2013) Ocular inflammation and infection. Emerg Med Clin North Am 31:387–397

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Granular Corneal Dystrophy Type 1 (GCD1), Groenouw Corneal Dystrophy Type I

► Stromal Dystrophies

Granular Corneal Dystrophy Type 2 (Granular-Lattice) (GCD2), Combined Granular-Lattice Corneal Dystrophy or Avellino Corneal Dystrophy

► Stromal Dystrophies

Granular Corneal Dystrophy Type I

► Groenouw Dystrophy Type 1 Disease

Granular Corneal Dystrophy, Type III

► Reis-Bücklers Dystrophy

Granular Dystrophy

► Corneal Dystrophies

Granular Keratinocytes

► Keratinocytes: Overview

Granulation Tissue-Type Hemangioma

► Pyogenic Granuloma

Graves Ophthalmopathy

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Synonyms

Dysthyroidal/thyroid-associated orbitopathy; Graves' orbitopathy; Thyroid eye disease

Definition

Graves disease (GD) is an autoimmune condition associated with hyperthyroidism. Thyroid eye disease (TED) is a disease of the orbit that typically presents with upper eyelid retraction, lid lag, swelling, erythema, conjunctivitis, and proptosis and can be associated with GD but is not unique to GD-related hyperthyroidism.

Epidemiology

GD occurs four times more often in females than in males. However, the prognosis for males is typically worse. Risk factors include age greater than 50, rapid onset of symptoms under 3 months, cigarette smoking, diabetes, hyperthyroidism, hyperlipidemia, and peripheral vascular disease.

History

Robert James Graves first described the disorder in 1835. The disease was associated with thyroid goiter and exophthalmos of the eye.

Clinical Features

TED is characterized by unilateral or bilateral upper eyelid retraction, lid lag in downward bilateral or unilateral proptosis, ophthalmoplegia, and sometimes compressive optic neuropathy.

Tests

After a complete ocular history and physical examination, if TED is suspected, then thyroid function studies (e.g., TSH, T3, T4) should be performed. Thyroid antibodies (e.g., TPO and TSIG antibodies) might also be helpful especially for confirming autoimmune hypothyroidism or in euthyroid patients. Orbital imaging including ultrasound, computed tomography (CT) scan, or magnetic resonance imaging (MRI) of the orbit can be done if there is diagnostic uncertainty. The distinctive radiographic sign of TED is enlargement of the extraocular muscles typically with sparing of the tendon. The most common order of involvement for the extraocular muscles in TED is inferior rectus, then medial rectus, then superior rectus, and lastly the lateral rectus muscles.

Differential Diagnosis

Previous eyelid surgeries
Third, fourth, or sixth cranial nerve palsy
Myasthenia gravis
Parinaud syndrome

Etiology

GD is a systemic autoimmune disorder in which antibodies are produced against the receptor for thyroid stimulating hormone (TSH). The abnormally high production of T3 and T4 may lead to an enlargement of the thyroid gland, seen as a goiter. It is postulated that the TSH receptor antibodies share a similar antigen that is present on the extraocular muscles. Therefore, TSH receptor and other thyroid-related antibodies bind to extraocular muscles and cause TED.

Diagnosis

GD is a clinical syndrome supported by laboratory and radiographic testing.

Treatment

The patient should consult with a medical internist or endocrinologist for management of the autoimmune thyroid disease. Conservative treatment for exposure keratopathy includes artificial tears and lubricating ointment. Elevation of the head of the bed might be useful for lid and orbital edema. Prednisone can be used to treat inflammatory TED and might reduce proptosis, corneal ulceration, acute disturbing double vision, and visual loss from optic neuropathy. Patients with compressive optic neuropathy due to TED however may require surgical decompression. In general, the surgical treatment of TED should follow a stepwise approach with orbital decompression first as this might change the pattern of strabismus, then strabismus surgery second as this might alter the lid position, and then eyelid surgery last.

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Graves' Disease

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Synonyms

Dysthyroid ophthalmopathy; Thyroid eye disease; Thyroid-associated orbitopathy

Definition

Graves' disease is an autoimmune inflammatory disorder that affects orbital and periorbital tissue. It is associated with hyperthyroidism at some point in most patients, although in less than 10% of cases, patients are hypothyroid or euthyroid.

Clinical Presentation

Graves' disease is always a bilateral process, although it is often asymmetrical. Many of the clinical signs and symptoms arise from soft tissue enlargement in the orbit including both extraocular muscles and adipose tissue. Patients under 40 years of age typically have a predominance of fat expansion, while patients over 60 years of age often have more extraocular muscle swelling. Although multiple muscles may be involved, the inferior rectus is the most common, followed by the medial rectus.

The most common symptoms include orbital pain or discomfort, diplopia, lacrimation, photophobia, and dry eye symptoms. The clinical

characteristic signs include lid retraction with temporal flare, lid lag, exophthalmos, restrictive extraocular myopathy, erythema of the periorbital tissues, or conjunctiva and corneal exposure. Three to five percent of cases are sight threatening due to optic nerve compression or corneal decompensation.

In patients with hyperthyroidism, pretibial myxedema and acropachy, which manifests as clubbing of the fingers or toes, may occur. The course of ophthalmopathy does not necessarily parallel the state of thyroid dysfunction.

Diagnosis

Diagnosis of thyroid abnormalities can be made with thyroid studies. Measurement of circulating thyrotropin-receptor antibodies may have diagnostic value due to their high specificity and sensitivity for Graves' disease. Orbital imaging with computed tomography (CT) or magnetic resonance imaging (MRI) may show fusiform extraocular muscle enlargement with sparing of the tendons and/or an increase in orbital fibroadipose tissue. Neuroimaging is particularly useful to evaluate optic nerve compression by enlarged muscles, especially at the orbital apex, known as apical crowding.

Differential Diagnosis

Orbital inflammatory syndrome, preseptal or orbital cellulitis, sarcoidosis, orbital metastases, dorsal midbrain syndrome, carotid-cavernous fistula.

Prophylaxis

Primary prevention of the disease is not feasible. However, the strongest modifiable risk factor is cigarette smoking, with a 7.7 odds ratio of developing the disease in smokers versus nonsmokers. Early and accurate control of thyroid dysfunction may also be important.

Therapy

Thyroid dysfunction should be treated if present with antithyroid medications or radioactive iodine. However, radioiodine therapy can cause progression of ophthalmopathy in about 15% of patients, especially in smokers and patients with severe hyperthyroidism, which may be prevented with concomitant treatment with oral prednisone.

Specific treatment depends on the severity of the disease. Patients with mild disease only require supportive therapy including ocular lubrication for dry eye or temporary prisms for diplopia.

For more severe disease, therapy is directed toward decreasing inflammation or acute orbital congestion with systemic corticosteroids or orbital radiotherapy, particularly for impaired motility.

Approximately 20% of patients require surgical intervention. Surgery is generally considered only after stabilization of the disease. Orbital decompression surgery is often done to restore normal globe position by expanding the orbital bony volume. Strabismus surgery and eyelid surgery to correct eyelid retraction may be indicated to correct diplopia and for cosmesis. If multiple surgeries are indicated, orbital decompression is done first, followed by strabismus surgery and then eyelid surgery.

Urgent intervention without waiting for stabilization may be needed to treat or prevent optic neuropathy or corneal decompensation by high-dose systemic corticosteroids, orbital radiotherapy, or orbital decompression.

Prognosis

Generally there is an initial active phase lasting 1–2 years, followed by stabilization. Only 5–10% of patients have reactivation of inflammation over their lifetime.

Smokers have a poorer prognosis, a longer duration of disease, and are less likely to respond to immunosuppressive therapy. Other poor prognostic features include male gender, older age,

rapidly progressive disease, and presence of dermopathy.

Epidemiology

Graves' disease has an annual incidence of 16 women and 3 men per 100,000 population. Two age peaks of incidence are observed in the fifth and seventh decade of life, varying slightly between men and women.

Cross-References

- ▶ Proptosis
- ▶ Retractors, Lower Eyelid

Further Reading

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Graves' Eye Disease

- ▶ Thyroid Eye Disease

Graves' Ophthalmopathy

- ▶ Thyroid Eye Disease

Graves' Orbitopathy

- ▶ Diplopia in Graves' Ophthalmopathy
- ▶ Graves Ophthalmopathy

Groenouw Dystrophy Type 1 Disease

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Synonyms

Granular corneal dystrophy type I

Definition

First described by German ophthalmologist Arthur Groenouw in 1890; Groenouw Dystrophy Type 1 is a bilateral, progressive, noninflammatory corneal condition marked by the development of focal anterior stromal opacities in a granular pattern.

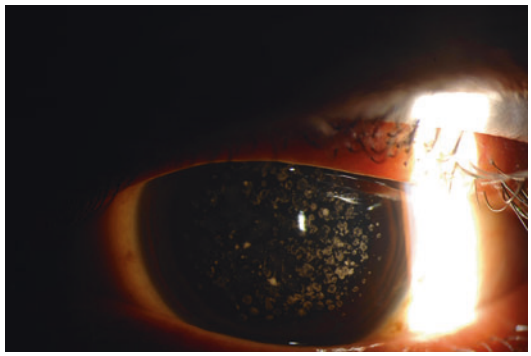
Etiology

A mutation in the TGFBI gene from Arg to Trp at position 555 in Chromosome 5q31 codes for keratoepithelin and is causative for Groenouw Dystrophy. It is inherited through autosomal dominant inheritance.

Clinical Presentation

Groenouw Dystrophy Type 1 often presents in childhood, affecting males and females equally. Patients are initially comfortable but may develop photophobia from light scattering and/or discomfort from recurrent corneal erosions. Visual acuity may be maintained for decades, until the disease has progressed to an advanced state.

On physical examination, central, fine, granular "bread crumb-," snowflake-, or ring-like lesions with empty intervening spaces present in the anterior stroma (Fig. 1). The peripheral cornea is often spared. With slit-lamp examination, lesions are opaque with direct illumination but translucent with retroillumination. Superficial



Groenouw Dystrophy Type 1 Disease, Fig. 1 Corneal photograph of a 37-year-old male with Groenouw Dystrophy Type 1, confirmed with genetic testing for the common TGFBI mutation

lesions may be associated with negative fluorescein staining.

Diagnosis

Diagnosis is primarily conducted by slit-lamp biomicroscopy. While focal lesions are generally round, lines may radiate from the individual lesions and should not be confused for lattice lines. Genetic testing for TGFBI mutations is commercially available and can help to differentiate Groenouw Dystrophy Type 1 from Avellino corneal dystrophy but is not necessary for diagnosis.

Histological evaluation of the cornea, conducted if corneal transplant is required, reveals strong, bright red staining of hyaline deposits with Masson Trichrome and weak staining with period acid-Schiff. These deposits may be eosinophilic, rod-like or trapezoidal in shape, and are appreciated anteriorly but can be deposited throughout the stroma.

Differential Diagnosis

Groenouw Dystrophy I differs clinically from Avellino corneal dystrophy (or granular-lattice corneal dystrophy) in that it is without lattice lines, although ray-like features in granular deposits may be deceiving in appearance. Both conditions originate from mutations in *TGFBI*. While both conditions demonstrate staining with Masson trichrome, amyloid deposits in Avellino corneal dystrophy stain positively with Congo Red. Laboratory genetic testing is beneficial in cases of a diagnostic dilemma.

Prophylaxis

None. Groenouw Dystrophy Type 1 is inherited; no known genetic therapy exists at this time.

Therapy

Many patients have few symptoms, requiring no treatment. Lubrication is helpful in the setting of recurrent corneal erosions.

In cases of advanced disease, surgical intervention is based on lesion depth, which can be measured with anterior segment optical coherence tomography. Superficial keratectomy or epithelial scraping can be utilized to address subepithelial deposits. Argon-fluoride excimer laser ablation may reduce or eliminate deposits in the anterior stroma, although vision may be limited by posterior lesions. Deep anterior lamellar keratoplasty or penetrating keratoplasty may be utilized in the setting of deep lesions.

Prognosis

Visual acuity is generally well maintained until middle age, but patients may present with severe disease at an earlier age, particularly those homozygotic for the mutation in TGFBI. Stromal haze may develop between hyaline granules in advanced disease, affecting visual acuity.

Phototherapeutic keratectomy in early-to-middle age maintains corneal transplantation as a future surgical option. Recurrence of Groenouw corneal dystrophy following corneal transplantation is common and independent of the size or type of graft. Lesions often re-appear superficially but may differ from primary presentation, appearing peripherally.

Epidemiology

Rare.

Cross-References

- ▶ Congenital Hereditary Stromal Dystrophy
- ▶ Crystalline Dystrophy
- ▶ Lattice Corneal Dystrophy

Further Reading

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Groenouw Dystrophy Type I

- ▶ Corneal Dystrophies

Guerin (Maxillary) Fracture

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Synonyms

Horizontal fracture; Le Fort I fracture; Maxillary fracture

Definition

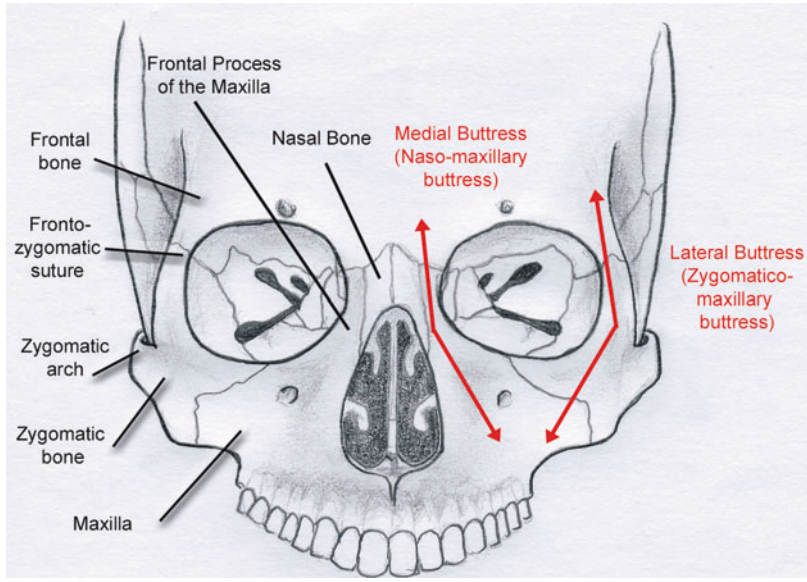
In 1901, Rene Le Fort categorized fracture patterns of the Maxilla resulting from a single blow to cadevaric skulls. The fracture lines, or "linea minoros resistentiae," described by Le Fort in 1901 are the basis for the modern Le Fort classification. The midface is attached to the cranium by three vertical buttresses that help distribute masticatory forces and stabilize the midface: the medial buttress (frontomaxillary buttress) and lateral buttress (zygomatico-maxillary buttress) anteriorly and the pterygomaxillary buttress posteriorly. The fractures described by Le Fort disrupt these buttresses. A Guerin fracture is equivalent to a Le Fort I fracture (also known as a horizontal fracture) and is a single horizontal fracture through the maxilla that passes through the septum medially, extending laterally through the pyriform rims, passing below the zygomatico-maxillary suture line, and transecting the pterygomaxillary junction to interrupt the pterygoid plates (Cummings 2005). Guerin fractures result in a mobile hard palate. It is important to realize that pure Guerin fractures are uncommon in clinical practice, and most midfacial fractures are an amalgam of various types of midfacial fractures (Figs. 1, 2, 3, and 4).

Etiology

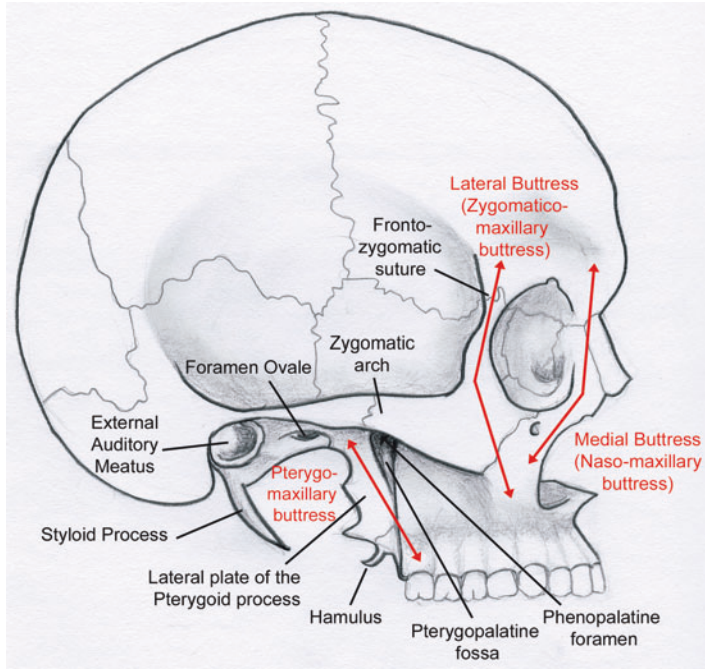
Guerin fractures are generally the result of blunt-force trauma to the midface. More specifically, Guerin fractures are most likely to occur after a blow to the inferior aspect of the maxilla, the maxillary alveolar ridge, directed downward. Common causes include motor vehicle accidents, interpersonal altercations, assaults, falls, and sports-related injuries.

Clinical Presentation

In the case of isolated Guerin fracture, overt clinical signs can be minimal (Papel 2002). Intraoral ecchymosis, lacerations, or palpable step-offs may be appreciated. The mobile bone

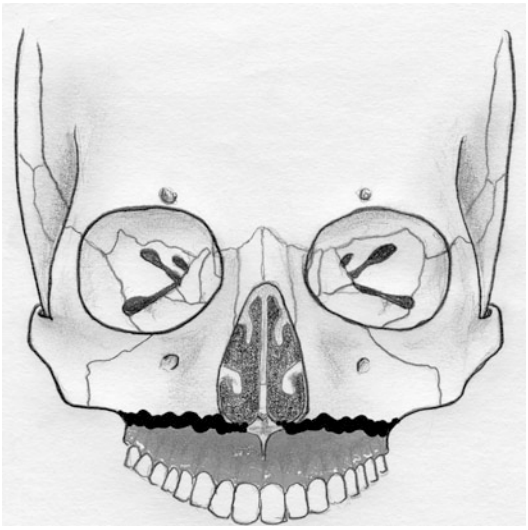


Guerin (Maxillary) Fracture, Fig. 1 Anteroposterior view of the vertical buttresses of the facial skeleton

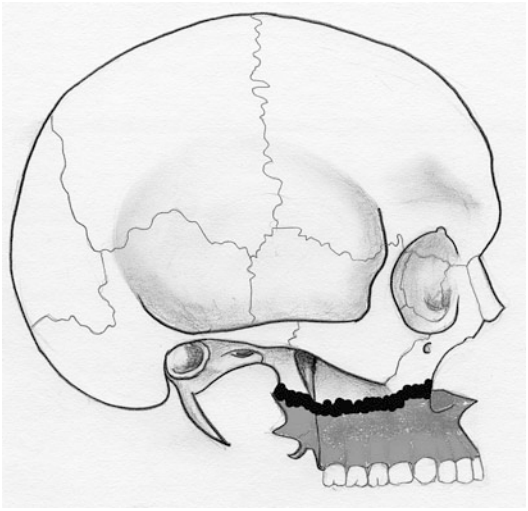


Guerin (Maxillary) Fracture, Fig. 2 Lateral view of the vertical buttresses of the facial skeleton

fragment resulting from a Guerin fracture tends to be driven posteroinferiorly along the slope of the skull base, resulting in malocclusion and an anterior open bite with posterior molars contacting before incisors. There may be crepitus at the gingival buccal sulcus from subcutaneous emphysema. Mobility of the hard palate at the pyriform rims can generally be appreciated. Palatal fractures and fractures of the dentoalveolar ridge may also occur. Significant facial edema is



Guerin (Maxillary) Fracture, Fig. 3 Anteroposterior view of a Guerin fracture (Le Fort I fracture or horizontal fracture). The *shaded area* represents the resultant mobile bone fragment



Guerin (Maxillary) Fracture, Fig. 4 Lateral view of a Guerin fracture. The *shaded area* represents the resultant mobile bone fragment

common with midfacial fractures, and it is important to keep in mind that presence of a Guerin fracture does not rule out presence of additional maxillofacial injuries.

Diagnostics

Maxillary fractures often occur as the result of significant trauma, and evaluation should begin with airway control and hemodynamic stabilization. Serious intracranial injury may be seen in up to 38% of patients with midfacial fractures; serious ophthalmologic injury may be seen in up to 28% of patients. Spinal cord injury should be ruled out, and any overt globe injury should be evaluated. A thorough history and physical, including a complete head and neck exam, may then be performed. With any midfacial fracture, suspicion for CSF rhinorrhea and/or otorrhea should be high. Examination of dental occlusion is important. Maxillofacial CT scan is considered the modality of choice for diagnosis of Guerin fractures.

Differential Diagnosis

Le Fort II fracture, Le Fort III fracture, naso-orbital-ethmoid fracture, zygomatico-maxillary complex fracture, palatal fracture.

Prophylaxis

The use of restraints, seat belts, and protective headgear can help prevent maxillary fractures.

Therapy

Treatment of ocular and CNS injuries should precede treatment of Le Fort fracture in the presence of a stable airway. Proper repair of complex midfacial fractures may require a surgical airway. When palatal fractures are present, the repair generally requires a custom-made reducing splint adapted to the palatal fragments and wired to the maxillary teeth. Palatal fractures should be reduced before plating of other maxillary fractures to ensure that proper dental occlusion is ultimately restored. Proper plating of Guerin fractures first requires mobilization of the resultant bone fragment and application of intermaxillary fixation

(Stewart 2005). Reconstruction and plating of disrupted facial buttresses is an important part of restoring normal occlusion and vertical height of the midface and stabilizing the midfacial skeleton against masticatory forces. Perioperative antibiotics should be considered in patients with facial fractures.

Prognosis

Long-term prognosis after repair of Guerin fractures is excellent. Postoperative infection rates are low and generally resolve with oral antibiotics.

Epidemiology

Maxillary (Guerin) fractures are most common in men aged 21–40.

Cross-References

- ▶ Le Fort Fractures
- ▶ Naso-Orbital-Ethmoid Fractures
- ▶ Orbit, Inflammation of
- ▶ Zygomatic Bone
- ▶ Zygomatic-Maxillary Complex Fractures

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Guerin Fracture (Le Fort I)

- ▶ Le Fort Fractures

Gul Schematic Eye

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Schematic eyes are used in theoretically modeling the real human eye as an optical instrument. The most popular schematic eye currently used is the Gullstrand model eye, which was proposed by Allvar Gullstrand and for which he received Nobel Prize in 1911. This model assumes all the ocular surfaces to be spherical and mentions their radius of curvatures. The model also mentions the thickness and refractive indices of different media inside the eye (the refractive indices are defined for 587 nm wavelength).

It was well known even at the time of Gullstrand that the representation of the eye as an optical system made up of spherical surfaces and homogeneous refractive index medium is a simplification. The profiles of all the ocular surfaces in reality are aspheric, and the refractive indices can have a spatial variation (gradient refractive index). The Gullstrand's model however has been popular in the vision science area over the last century as it serves well for paraxial calculations. There are four different Gullstrand model eyes that are currently being used.

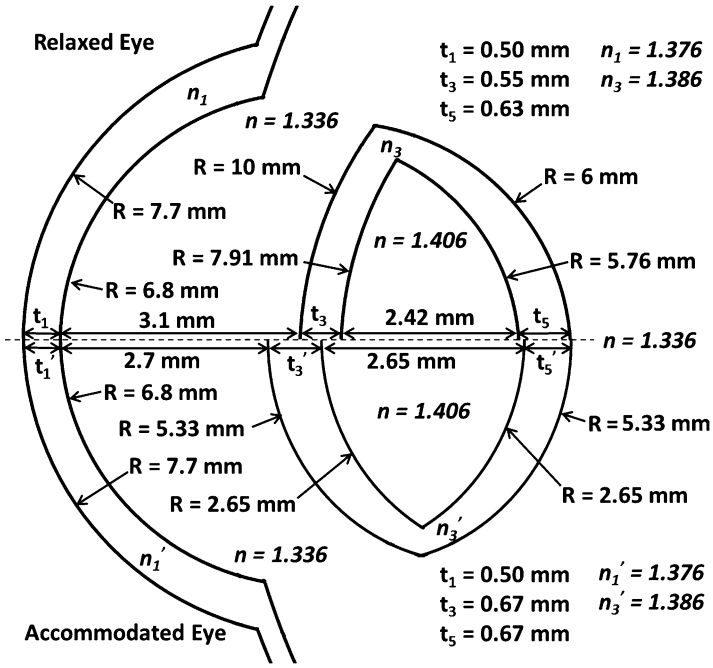
1. Gullstrand exact eye or Gullstrand eye #1
2. Simplified Gullstrand eye or Gullstrand eye #2
3. Gullstrand-Emsley eye
4. Gullstrand-Legrand eye

Gullstrand Exact Eye

Gullstrand exact eye is a detailed representation of the eye; it assumes the eye's optical system to be having six surfaces. The cornea in this model is described to be a two-surface element with finite thickness. The lens is described to

Gul Schematic Eye, Table 1 Structural parameters of Gullstrand exact eye

	Relaxed eye			Accommodated eye		
Surface	Radius (mm)	Thickness (mm)	Refractive index	Radius (mm)	Thickness (mm)	Refractive index
Anterior cornea	7.7	0.5	1.376	7.7	0.5	1.376
Posterior cornea	6.8	3.1	1.336	6.8	2.7	1.336
Anterior lens surface	10	0.55	1.386	5.33	0.67	1.386
Anterior lens nucleus	7.91	2.42	1.406	2.65	2.65	1.406
Posterior lens surface	−5.76	0.63	1.386	−2.65	0.67	1.386
Anterior lens nucleus	−6	17.18	1.336	−5.33	16.8	1.336
Image	−17.2			−17.2		



Gul Schematic Eye, Fig. 1 Gullstrand exact eye schematic

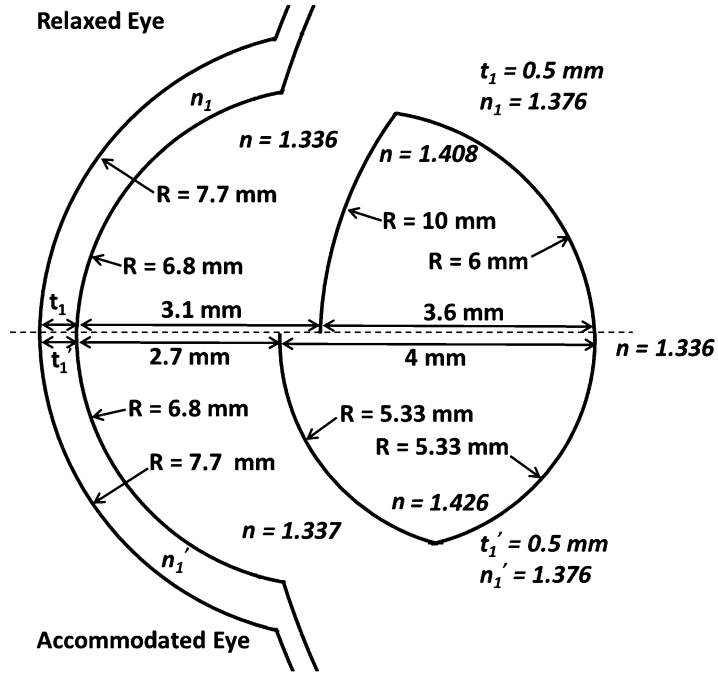
have an inner nucleus and outer shell thus making it a four-surface element. The model describes the eye in both relaxed and accommodated states. Table 1 gives the details on the dimensions and refractive indices for the relaxed and accommodated Gullstrand exact eye. Figure 1 shows the schematic of the Gullstrand exact eye.

Simplified Gullstrand Eye

This model is a simplified version of the Gullstrand exact eye, which assumes the eye's optical system to have four surfaces. The cornea in this model is the same as in the exact eye, while the crystalline lens is simplified to a two-surface element. Table 2 shows the structural parameters of

Gul Schematic Eye, Table 2 Structural parameters of simplified Gullstrand eye

	Relaxed eye			Accommodated eye		
Surface	Radius (mm)	Thickness (mm)	Refractive index	Radius (mm)	Thickness (mm)	Refractive index
Anterior cornea	7.70	0.50	1.376	7.70	0.50	1.376
Posterior cornea	6.80	3.10	1.336	6.80	2.70	1.336
Anterior lens surface	10.00	3.60	1.408	5.33	4.00	1.426
Posterior lens surface	−6.00	17.18	1.336	−5.33	13.82	1.336
Image	−17.20			−17.20		



Gul Schematic Eye, Fig. 2 Relaxed simplified Gullstrand eye schematic

this model. Figure 2 shows the schematic of the simplified Gullstrand eye.

Gullstrand-Emsley Eye

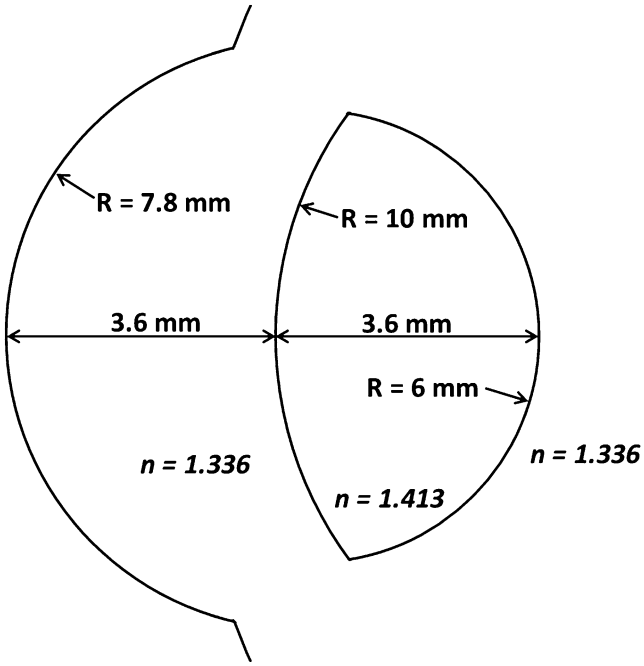
This model further simplifies the Gullstrand model by providing a three-surface representation of the eye where the cornea is assumed to be a single surface and the lens is assumed to be a two-surface optical element. Accommodated state of the eye is not described in the model. Table 3 shows the structural parameters of the model, while Fig. 3 shows the schematic of the Gullstrand-Emsley model eye.

Gullstrand-Legrand Eye

Gullstrand-Legrand eye is perhaps the most widely used Gullstrand model and is inspired from the simplified Gullstrand eye. As in simplified Gullstrand eye, this model also assumes the eye's optical system to have four surfaces,

Gul Schematic Eye, Table 3 Structural parameters of Gullstrand-Emsley eye

Surface	Radius (mm)	Thickness (mm)	Refractive index
Cornea	7.8	3.6	1.336
Anterior lens surface	10	7.2	1.413
Posterior lens surface	−6	17	1.336
Image	–		

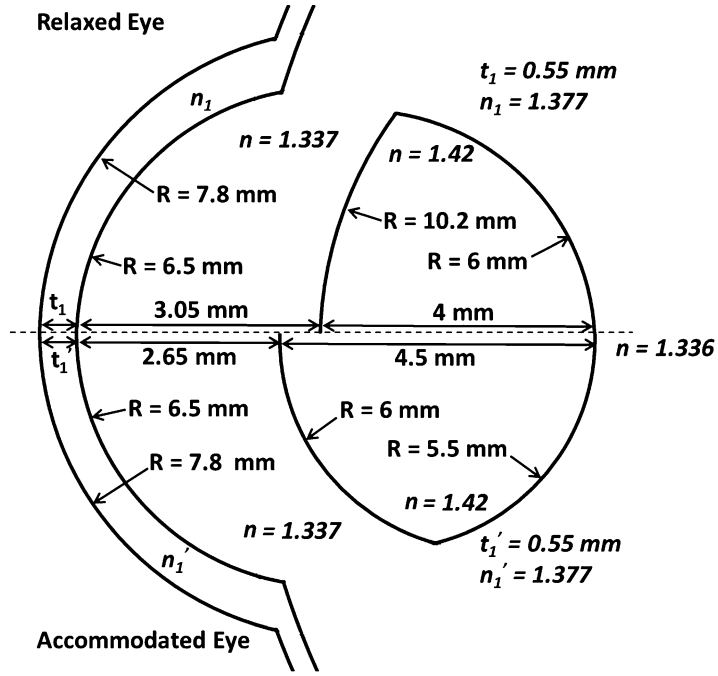


Gul Schematic Eye, Fig. 3 Schematic of the Gullstrand-Emsley eye

Gul Schematic Eye, Table 4 Structural parameters of Gullstrand-Legrand eye

	Relaxed eye			Accommodated eye		
Surface	Radius (mm)	Thickness (mm)	Refractive index	Radius (mm)	Thickness (mm)	Refractive index
Anterior cornea	7.8	0.55	1.377	7.7	0.55	1.377
Posterior cornea	6.5	3.05	1.337	6.5	2.65	1.337
Anterior lens surface	10.2	4	1.42	6	4.5	1.42
Posterior lens surface	−6	16.6	1.336	−5.5	14.23	1.336
Image	−17.2			−17.2		

two for the cornea and two for the crystalline lens. The curvature, thickness, and refractive index values however are different. This model also describes both relaxed and accommodated states. Table 4 shows the structural parameters of the model. Figure 4 shows the schematic of the Gullstrand-Legrand model eye.



Gul Schematic Eye, Fig. 4 Schematic of the Gullstrand-Legrand model eye

Cross-References

- ▶ Accommodation, Cataract
- ▶ Cornea
- ▶ Crystalline Lens

Further Reading

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Gunn Pupillary Test

- ▶ Swinging-Light Test, for RAPD Identification

Gyrate Atrophy of the Choroid and Retina

- ▶ Atrophy, Gyrate

Gyrate Atrophy of the Retina and Choroid

- ▶ Choroid, Gyrate Atrophy of

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Haemophilus influenzae, Conjunctivitis

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Synonyms

Bacterial conjunctivitis; Pink eye

Definition

Haemophilus influenzae is a causative bacterial agent responsible for acute and purulent conjunctivitis, or inflammation of the conjunctiva.

Structure

Haemophilus influenzae is a small pleomorphic, gram-negative coccobacillus (Cherry et al. 2014). This organism is nonmotile, non-spore forming, and facultatively anaerobic. H influenzae is unique in that it requires growth supplementation, factor X and V. There are roughly eight biotypes and six serotypes (Tindall 2008). The eight biotypes are categorized by the presence or absence of indole, urease, and ornithine decarboxylase. The serotypes (a–f) are based upon the type of polysaccharide capsule around the organism. Unencapsulated forms of the organism also exist. These unencapsulated forms typically cause a variety of mucosal infections, including conjunctivitis (Cherry et al. 2014).

Function

The bacteria colonize the human respiratory tract (Tindall 2008). Asymptomatic colonization may be present. Transmission occurs through direct contact with or inhalation of respiratory secretions. Mucosal infections involve movement of H influenzae through the nasal ostia to the sinuses and up the Eustachian tubes (Cherry et al. 2014). Infection of the eye may occur

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following this transmission after an episode of sinusitis or otitis media.

Clinical Relevance

Prior to the development of H influenzae type b vaccine, H influenzae was an important cause for several bacterial infections (Tindall 2008). Related ophthalmic diseases include conjunctivitis and orbital cellulitis. H influenzae carries increased transmission and risk among pediatric populations. Children are at increased risk in centers such as day-care or nurseries.

Diagnosis of conjunctivitis secondary to H influenzae is made via clinical presentation and laboratory findings. Patients with a recent history of upper respiratory infection, sinusitis, or sinus surgery are at increased risk for H influenzae-associated conjunctivitis (Tindall 2008). Patients may have symptoms of eye redness, pain, blurred vision. Laboratory findings include positive gram stain and culture growth. Of note, chocolate agar medium is required for this organism.

Once identified, treatment for conjunctivitis is topical fluoroquinolone eye drops ranging from four times per day to hourly depending on disease severity (Tindall 2008).

Cross-References

► *Cellulitis, Preseptal, Haemophilus Causing*
► Conjunctivitis

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Hallucination

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Definition

A hallucination is a sensory perception lacking the appropriate real external stimulus of that sensory system, including any of the five senses. Visual hallucinations (VH), in particular, might occur as the result of various underlying neurological etiologies, or they might occur as an isolated instance without defect of cognition or mental function.

Etiology

A hallucination, simple or complex, can be a symptom of many underlying causes.

Hallucinations may be present as a symptom of a dementia (e.g., Alzheimer's), confusion (e.g., epilepsy, delirium, stroke, alcohol withdrawal), or psychiatric etiologies (e.g., schizophrenia, narcolepsy). Hallucinations with these origins might involve multiple sensory systems (multimodal hallucinations) as well as other symptoms of the underlying mental illness.

Drugs as well as some metabolic disorders have been known to cause visual hallucinations. Drugs, such as MDMA or 3,4-methylenedioxymethamphetamine (aka "ecstasy") or lysergic acid diethylamide (LSD), are "hallucinogens" that can result in VH or other perception disturbances. Likewise, dopamine agonists, serotonin agonists, atropine, and other prescription drugs can also result in VH. Metabolic disorders such as Niemann-Pick disease, α-mannosidosis, or urea cycle defects have been known to cause VH.

Patients with intact mental and cognitive function who experience visual hallucinations may fall into one of three main pathophysiologic groupings of VH: (1) release hallucinations (e.g., Charles Bonnet syndrome due to visual loss), (2) seizures (e.g., temporal or occipital lobe seizures), and (3) migraine aura (see ▶ Charles Bonnet Syndrome: Overview, and ▶ Occipital Seizures: Transient Visual Loss).

History

The description of what is clinically considered a hallucination is prevalent in the earliest known medical writings. However, the first modern use of the term hallucination was defined by Jean-Etienne Esquirol in his book *Des Maladies Mentales* in 1837.

Clinical Presentation

Depending on the type of VH, presentation can range from seeing spots and patterns to seeing complex visual images as detailed as people or animals. Various etiologies can result in a large variety of associated symptoms with VH including migraine hallucinations (visual aura) with a severe unilateral headache or complex VH with few other associated symptoms (see ▶ Peduncular Hallucinosis).

Treatments

Treatments for VH should be directed at the underlying etiology.

Prognosis

The expected recovery of the VH depends on the underlying etiology and its respective treatments.

Epidemiology

Recent studies combining surveys from various countries, including the United States, Germany, and Italy, have determined the prevalence of VH in the general population to be 7.3%. When drug-induced VH and VH as a result of physical illness were excluded from this combination of surveys, the general population still exhibited a VH prevalence of 6%. VH is also known to be a common symptom in psychotic disorders, such as schizophrenia (27%) or bipolar and affective disorder (15%). There has been contradictory information regarding the prevalence of VH in men versus women in the general public. With regard to age, there is a bimodal distribution of the greatest incidence of VH during a lifetime: first in late adolescence/early adulthood and second in late life. The late adolescent/early adulthood peak is related to the higher incidence of psychosis, while the late in life peak correlates with a higher incidence of brain and eye diseases with VH as a symptom.

Cross-References

▶ Charles Bonnet Syndrome: Overview
▶ Drugs: Hallucinations

▶ Occipital Seizures: Transient Visual Loss
▶ Peduncular Hallucinosis

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Hallucinogen

▶ Drugs: Hallucinations

Hamartoma

▶ Trichofolliculoma

Hand-Held Infrared Pupillometer

▶ Colvard Pupillometer

Hanot-Chauffard Syndrome

▶ Hemochromatosis

Hansen's Disease

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Synonyms

Leprosy

Definition

Chronic granulomatous inflammation of the peripheral nerves, skin, and mucus membranes caused by the intracellular bacteria *Mycobacterium leprae*.

Etiology

Hansen's disease is caused by the *M. leprae* bacteria which is only mildly contagious. The intracellular bacteria infect the eye and other parts of the body by direct inoculation and primarily reside in peripheral, cutaneous nerves. *M. leprae* shows a predilection for the cutaneous Schwann cells and grows best at lower temperatures of 27–30 °C. *M. leprae* down-regulates myelin gene expression in nerves and this process eventually results in peripheral neuropathy. *M. leprae* also causes a chronic granulomatous inflammation that damages local organs and structures (Nunzi and Massone 2012).

The spectrum of disease, classified by the Ridley-Jopling classification system, depends on the patient's unique immune system and response to the bacteria, which is determined by each patient's human leukocyte antigen (HLA) composition. Responses range from tuberculoid leprosy (TT), characterized by a strong inflammatory response and few bacteria, to lepromatous leprosy (LL) marked by minimal inflammatory response

and ample bacteria. Any inflammatory response with signs of both TT and LL leprosy is designated as "borderline." There are also two subtypes of leprosy-related inflammatory responses: type 1, primarily T-cell-mediated delayed hypersensitivity, and type 2, primarily B-cell-mediated humoral response based on antigen-antibody complex deposition. TT is associated with a type 1 reaction and LL is associated with a type 2 reaction. While most patients have predominantly a type 1 or type 2 inflammatory response, a switch in the type of inflammation, known as a "reversal reaction," can occur spontaneously during the disease course or as a result of the initiation of multidrug therapy (Hussein and Schwab 2013).

Clinical Presentation

Clinically, it is generally rather easy to distinguish between the polar forms of tuberculoid leprosy and lepromatous leprosy. Tuberculoid leprosy presents with mostly local symptoms confined to the skin. These lesions are hypopigmented macules with raised edges and no nerve sensation resulting in anhidrosis and anesthesia. In contrast, lepromatous leprosy presents with systemic symptoms and is much more severe than the tuberculoid form. There is greater nerve involvement and subsequently greater disability. Signs and symptoms of lepromatous leprosy are a result of nerve demyelination and chronic granulomatous inflammation and differ depending on the body part affected. There are confluent papules and nodules and diffuse infiltration of the skins resulting in leonine facies and madarosis (Eichelmann et al. 2013). Diffuse deposition of immune complexes can lead to fever, malaise, painful erythematous skin nodules, and multi-organ involvement, including the eye. It is far more common for patients with lepromatous leprosy to have ocular involvement than tuberculous leprosy patients (Yanoff and Duker 2009).

Peripheral neuropathy and granulomatous inflammation are responsible for the ocular pathology present in patients with Hansen's disease. Neuropathy can affect both motor and sensory nerves. In the ocular adnexa and ocular surface, demyelination of superficial branches of cranial nerves V and VII cause ectropion, lagophthalmos, and anesthetic corneas with decreased blink reflex, leading to greater susceptibility to exposure keratitis and corneal ulceration (Nunzi and Massone 2012). Denervation of the lacrimal gland results in xerophthalmia or aqueous tear deficiency dry eye. Nonreactive pinpoint pupils occur with denervation of iris dilator muscles and parasympathetic denervation causes difficulties in accommodation. Thickened edematous corneal nerves on exam are pathognomonic of leprosy (Hussein and Schwab 2013).

Granulomatous inflammation in the ocular adnexa leads to destruction of hair follicles and meibomian glands resulting in eyebrow loss, madarosis, and lipid deficiency dry eyes. Dacryocystitis occurs with bacterial invasion of the nasolacrimal duct. Within the eye, miliary lepromas cause punctate keratitis and subepithelial immune infiltrates that can coalesce and obscure vision. Corneal lepromas occur at the limbus or sclera, most commonly at the cooler interpalpebral fissure, and can extend across the cornea. Scleral thinning, scleromalacia, and staphylomas occur with chronic granulomatous inflammation. Iris pearls are pathognomonic for ocular leprosy, arising near the pupil edge, and can coalesce, detach, and obstruct the angle. Recurrent iritis can result in iris atrophy and synechia (scar) formation (Hussein and Schwab 2013). Ultimately, mild chronic uveitis and complex cataract formation is the principal cause of blindness (Nunzi and Massone 2012).

Diagnosis

Hansen's disease can be clinically diagnosed if a patient has not completed a treatment regimen for leprosy and has one or more of three cardinal signs including (1) a hypopigmented or erythematous skin lesion with sensory loss, (2) a thickened peripheral nerve, or (3) a positive skin smear or acid-fast bacilli observed in a biopsy. The diagnostic sensitivity of all three cardinal signs that are present has been shown to be as high as 97%. Corneal scrapings can confirm ocular

involvement as well as anterior chamber or vitreous taps showing acid-fast bacilli (Eichelmann et al. 2013).

Differential Diagnosis

Tuberculosis
Brucellosis
Sarcoidosis

Prophylaxis

M. leprae is mildly communicable and thought to be spread from person to person via respiratory droplets. Overcrowding and prolonged contact with infected individuals are known risk factors for developing the disease (Hussein and Schwab 2013). Armadillos are the only other known reservoirs for *M. leprae* and thus avoidance should be advised though transmission is rare (Eichelmann et al. 2013).

The BCG vaccine, developed against *Mycobacterium tuberculosis* has been shown to bestow up to 50% protection against *Mycobacterium leprae*. When heat-inactivated *M. leprae* organisms are added to the vaccine, up to 64% resistance is conferred (Eichelmann et al. 2013).

Therapy

Primary therapy includes rifampicin and dapsone for 6 months for tuberculous leprosy. In patients with lepromatous leprosy, clofazimine is added to the regimen and therapy is extended to 12 months (Hussein and Schwab 2013). A combination of medications is used to prevent emergence of drug resistance and quickly reduce the chances of transmission. Second-line therapy includes minocycline, ofloxacin, and clarithromycin, which have been shown to be more efficacious, yet use is limited due to higher cost. Initiation of multidrug therapy often results in a "reversal reaction," a brisk inflammatory response that needs to be controlled with a prolonged course of systemic prednisone or thalidomide (Eichelmann et al. 2013).

Prognosis

Prognosis is dependent on the stage of disease and extent of neuropathy at the time of diagnosis. Ocular pathology increases with disease duration; therefore, early diagnosis and treatment leads to a better outcome (Malik et al. 2011).

Epidemiology

In 2011 almost 220,000 new cases of leprosy were detected worldwide, the vast majority in Southeast Asia (Global 2012). Sight-threatening ocular complications are seen in approximately 20% of patients, the vast majority being patients with lepromatous leprosy (Malik et al. 2011).

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Haptic

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Synonyms

Intraocular lens haptics

Definition

Haptic means relating to or based on the sense of touch. With regard to the design of an intraocular lens, haptic is the part of the lens that does not take part in focusing light but holds the lens in place (Kohnen and Koch 2009).

Epidemiology

Every intraocular lens (IOL) consists of an optic and a haptic.

Clinical Features

IOL haptics material can be made of polypropylene, polyvinylidene fluoride homopolymer, polyamide, PMMA, silicone, or acrylic. If the optic of the IOL is made of the same material as the haptic, the IOL is a single-piece IOL, if haptic and optic are made of two different materials, the IOL is a three-piece IOL. Generally, "plate"-haptics, "C"-haptics, "loop"-haptics, and "three"- or "four"-point haptics are differentiated. The term angulation refers to the angle between the optic of the IOL and the haptic (Werner 2008; Kohnen et al. 2009).

Tests

In biomicroscopic evaluation of an implanted IOL, the type of haptic can usually be assessed.

Differential Diagnosis

Every intraocular lens has an optic and a haptic.

Etiology

The term haptik refers to Greek "haptein" which means "to touch."

Treatment

In scope of aphakic, pseudophakic, or phakic IOL implantation, the haptic is inserted in the capsular bag, ciliary sulcus, anterior chamber angle, or enclavated in the iris.

Cross-References

- ▶ Acrylic IOL
- ▶ Cataract Surgery
- ▶ Intraocular Lens
- ▶ Off-Center Optics
- ▶ Phakic Intraocular Lens

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Hard Palate Graft

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Synonyms

Eyelid spacer graft; Tarsal substitute

Definition

Free graft of hard palate taken from the oral cavity and transplanted to the lower eyelid as a spacer graft and substitute for posterior lamellar (conjunctiva and tarsus) replacement, and as a posterior and middle lamellar (orbital septum) stent in postsurgically retracted lower eyelids.

Indication

Utilized in lower eyelid reconstruction for posterior lamella (conjunctiva and tarsus), inadequacy secondary to eyelid cancer excision, trauma, or congenital defects. Also, used as a posterior/middle lamellar stent in the repair of postsurgical lower eyelid retraction and scleral show.

Contraindication

Patients with significant oral disease may not be adequate donors. Hard palate is usually avoided as a tarsal replacement in the upper eyelid because of the presence of keratinized epithelium, which can abrade the cornea.

Techniques and Principles

Assessment of the degree of posterior lamellar inadequacy or the degree of lower eyelid retraction and scleral show is performed and the proper graft size determined. The graft is harvested from the hard palate between the midline raphe and the gingival surface of the teeth, avoiding the soft palate posteriorly. The donor site is left to heal by secondary intention; however, placement of a prefabricated dental stent can help minimize postoperative discomfort. The graft is then trimmed and thinned with scissors to the desired size. The graft is sutured in place, mucosal surface toward the globe, with absorbing sutures to reconstruct the posterior lamellar defect. In cases of lower eyelid retraction, the graft is sutured to the lower border of the tarsus superiorly and the cut edge of conjunctiva inferiorly. The lower eyelid is usually placed on upward stretch for 1 week with Frost sutures to facilitate healing and avoid corrugation of the graft.

Outcome

The hard palate graft undergoes a variable degree of contraction postoperatively but usually provides for long-term posterior lamellar replacement and/or middle lamellar support.

Complications

Graft failure and slough with contraction and failure to reconstruct the eyelid are possible. Donor site infection is also possible. Corneal irritation and possible abrasion from the keratinized epithelium, particularly when utilized as a tarsal replacement, can occur.

Cross-References

▶ Reconstructive Surgery of Eyelid
▶ Spasm of Eyelids

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Hartmann-Shack Wave Front Sensing

► Shack-Hartmann Aberrometry

Hassall-Henle Bodies

► Peripheral Corneal Guttata (Hassall-Henle Bodies/Warts)

Hassall-Henle Warts

► Peripheral Corneal Guttata (Hassall-Henle Bodies/Warts)

Heat Injury

► Thermal Injury: Overview

Heerfordt's Syndrome

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Synonyms

Uveoparotid fever

Definition

Heerfordt's syndrome is a rare form of sarcoidosis in which patients present with fever, uveitis, parotitis, and/or seventh nerve palsy.

Etiology

As a rare form of sarcoidosis, the etiology for Heerfordt's syndrome disease is unknown. The disease process involves T-cell-mediated granulomatous inflammation.

Clinical Presentation

Heerfordt's syndrome usually presents acutely in younger patients with uveitis, fever, parotitis, and cranial nerve palsy, usually involving the seventh cranial nerve. With this facial nerve palsy, the patient may have incomplete closure of the eyelids on the affected side and may be unable to purse one's lips. The patient's parotid glands are generally firm and nontender. Patients may also have enlargement of the submandibular and lacrimal glands.

Patients may have other system signs of sarcoidosis such as skin lesions, pulmonary disease, and other less common manifestations such as neurological disease, arthritis, bone cysts, renal disease, lymphadenopathy, splenomegaly, liver disease, and cardiac arrhythmias. Pulmonary disease can manifest as bilateral asymptomatic hilar lymphadenopathy, diffuse reticulonodular infiltrates, or even pulmonary fibrosis which may result in pulmonary hypertension and cor pulmonale. Skin lesions may manifest as erythema nodosum, scattered plaques or nodules, lupus pernio, or deposits in long-standing scars.

Patients with Heerfordt's syndrome also may have ocular involvement most often presenting as uveitis. However, other ocular manifestations include keratoconjunctivitis sicca, conjunctival nodules, and, very rarely, scleral or orbital lesions. Patients can have an acute anterior uveitis or a chronic granulomatous uveitis. Patients with intermediate uveitis may present with snowballs. Other patients may have periphlebitis which would appear as yellowish or gray-white perivenous sheathing which can sometimes also involve the optic nerve. Severe periphlebitis will result in perivenous exudates called candlewax drippings. Although rare, choroidal infiltrates can present as many small, pale yellow "punched out" infiltrates, multiple large confluent lesions with amoeboid

margins, or exceedingly rarely as solitary choroidal granulomas. Other ocular findings can include retinal granulomas, peripheral retinal neovascularization secondary to retinal capillary drop out, a nummular keratitis, and optic nerve involvement. Optic nerve involvement could include focal granulomas by the optic nerve, papilledema secondary to central nervous system involvement, or persistent disk edema associated with vitreous or retinal involvement.

Diagnosis

Although only 6% of patients with sarcoidosis present with parotid involvement, the additional presenting symptoms of fever, uveitis, and facial nerve palsy make Heerfordt's syndrome extremely likely. Ultrasound-guided biopsy of the enlarged parotid glands may be utilized for histologic diagnosis, but other involved glands may be biopsied instead.

For a diagnosis of sarcoidosis, enzyme assays of angiotensin-converting enzyme (ACE) and lysozyme levels in addition to biopsy are common methods used to arrive at this diagnosis of exclusion. Lung biopsy is the highest yield (90%). This is so even in asymptomatic patients with a normal chest X-ray. In patients with conjunctivitis with conjunctival nodules, biopsies are positive 70% of the time. In enlarged lacrimal glands, biopsies are positive 75% of the time, but in un-enlarged lacrimal glands, biopsy yield can be as low as 25%. Pulmonary function tests would show a restrictive lung disease pattern. A strongly positive Mantoux test to a tuberculin unit would make a diagnosis of sarcoidosis less likely. Chest radiographs will be abnormal in patients with general sarcoidosis 90% of the time.

Differential Diagnosis

The constellation of signs and symptoms of fever, parotitis, seventh nerve palsy, and uveitis makes Heerfordt's Syndrome extremely likely. However, other diagnoses such as lymphoma should be ruled out with ultrasound biopsy of the enlarged parotid glands.

Differential diagnosis of posterior segment sarcoidosis is organized into small choroidal lesions, large choroidal infiltrates, and periphlebitis. Small choroidal lesions could also be tuberculosis, birdshot chorioretinopathy, or multifocal choroiditis with panuveitis. Findings of large choroidal infiltrates could also be large cell lymphoma, Harada disease, serpiginous choroidopathy, or metastatic tumor. Finally, other causes of periphlebitis could be Behcet syndrome, tuberculosis, or cytomegalovirus retinitis.

Prophylaxis

There is no prophylaxis for this disease.

Therapy

Therapy would be the same for sarcoidosis, generally high-dose steroids such as starting the patient on 60 mg per day of prednisone. Topical and/or periocular steroids would also be used for any anterior uveitis. If the patient has posterior uveitis, then the systemic steroids given for the systemic involvement in Heerfordt's syndrome would be of benefit as well. The patient may also require immunosuppressive agents such as methotrexate, cyclosporine, or azathioprine. Cyclophosphamide and infliximab have been shown to be useful in refractory disease as well.

Prognosis

Prognosis is generally good if patient has timely diagnosis and treatment. However, if the patient also presents with the multifocal choroiditis, then visual prognosis is especially guarded as the patient may develop choroidal neovascularization resulting in loss of central vision or a chorioretinal scar.

Epidemiology

Only 6% of patients with sarcoidosis present with parotid involvement. When the patient also has the other constellation of signs and symptoms of fever, uveitis, and/or facial nerve palsy, then the disease is called Heerfordt's syndrome. In regard to sarcoidosis, patients are more commonly of African rather than Caucasian descent. Patients with Heerfordt's syndrome are more commonly younger patients who present acutely.

Cross-References

► Sarcoidosis

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Helical Computed Tomography

► Spiral Computed Tomography, in Orbital Evaluation

Heliophobia

► Day Blindness (Hemeralopia), in Cone Dystrophies

Hemangiectatic Hypertrophy

► Klippel-Trenaunay-Weber Syndrome

Hemangioblastomas, with Retinal Angiomatosis (von Hippel Lindau Disease)

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Synonyms

Angiomatosis retinae; Cerebelloretinal hemangioblastomatosis; Familial cerebello-retinal angiomatosis; Hippel Disease; Hippel–Lindau syndrome, HLS; Lindau disease or retinocerebellar angiomatosis; Retinal hemangioblastomas; Von Hippel-Lindau disease, VHL

Definition

See the main entry "► Familial Cerebello-Retinal Angiomatosis."

Cross-References

► Retinae (Retinal Angiomatosis, von Hippel Syndrome/Disease)
► Familial Cerebello-Retinal Angiomatosis

Hemangioma

► Port-Wine Stain (Nevus Flammeus)

Hemangiopericytoma

► Vascular Tumors Disease of the Conjunctiva

Hematoma

► Eyelid Trauma

Hemochromatosis

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Synonyms

Hanot-Chauffard syndrome; Iron overload

Definition

Hemochromatosis is a systemic disorder of iron overload leading to eventual organ dysfunction.

Etiology

Primary hemochromatosis is the most common type of hemochromatosis and is due to autosomal recessive missense mutations on short arm of chromosome 6 in *HFE*. This gene encodes for an MHC class 1-like molecule that binds with transferrin receptor and affects hepcidin homeostasis. The subsequent defect of this pathway leads to increased iron absorption in the upper gastrointestinal tract, leading to iron deposition in parenchymal cells of the liver, heart, pancreas, joints, and endocrine organs.

The C282Y mutation is the most frequently identified causative genetic lesion, for which homozygosity confers the disease state. Patients heterozygous for this allele are carriers but generally do not demonstrate clinical disease. The exception is the compound heterozygote; carriers who also have the H63D mutation, prevalent among individuals of North Italian descent, may develop a milder form of iron overload. The homozygous C282Y mutation affects 5 in 1000 individuals with northern European descent.

Secondary hemochromatosis may also occur due to iron overload from external sources such as multiple blood transfusions, thalassemia, sickle cell anemia, or increased iron intake.

Occurrence

Hemochromatosis is a systemic disease with multi-organ involvement. Clinical symptoms generally appear between 40 and 60 years of age and primarily in homozygous males.

Externally, the location of deposits is found most frequently in an interpalpebral distribution. It may be found at the lid margins and is often present in both the upper and lower lids. Discoloration of the bulbar conjunctivae has been reported to occur in approximately 20% of patients, and rust-colored deposits may be appreciated within insertions of the recti muscles and sclera. The intervening conjunctival lymphatic channels render a radially striated appearance of the deposited pigments (Lazzaro et al. 1998).

In the cornea, iron deposits appear as fine dusting of the subepithelial and anterior stromal space, inferiorly greater than superiorly. A clear zone of 1.5 mm appears between deposits and the limbus. In an otherwise normal eye, these deposits are more broadly distributed in contrast to the iron lines seen with aging (Hudson-Stahli line), at the base of the cone in keratoconus (Fleischer ring), at the edge of a filtering bleb (Ferry line), or at the head of a pterygium (Stocker line).

Histopathological evaluation of eyes in patients with hemochromatosis postmortem reveals scattered iron granules deposited in the ciliary body, sclera, and iris, with an absence of iron in the choroid or retina. Although iron deposition has been noted in the peripapillary retinal pigment epithelium, these cases also have sparing of the neurosensory retina and choroid (Roth and Foos 1972).

Systemically, the diagnosis of hemochromatosis is often accompanied by arthralgia, fatigue, amenorrhea, infertility, and impotence and associated with hepatomegaly and cirrhosis. Approximately 85% of cirrhotic patients also develop secondary diabetes (known as "bronze diabetes") and are at risk for associated intraocular retinopathy. Dermatologic manifestation includes a characteristic bronze appearance of the skin.

Classification

Hemochromatosis may be primary (hereditary hemochromatosis, HH) or secondary (acquired hemochromatosis) in origin. This should be distinguished from hemosiderosis secondary to an iron-based intraocular foreign body.

Cross-References

- ▶ Hudson-Stähli Line
- ▶ Iron Lines, Pterygium
- ▶ Iron, Corneal Deposits of
- ▶ Iron, Corneal Intraocular Foreign Body of
- ▶ Siderosis: Signs and Symptoms

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Hemorrhagic Viral Keratoconjunctivitis

▶ Acute Hemorrhagic Conjunctivitis

Hepatolenticular Degeneration

▶ Wilson Disease

Hereditary Crystalline Stromal Dystrophy of Schnyder

▶ Schnyder Crystalline Dystrophy Syndrome

Hereditary Gelsolin Amyloidosis

▶ Meretoja Syndrome

Hereditary Hemorrhagic Telangiectasia (Osler-Weber-Rendu Disease)

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Synonyms

Osler-Weber-Rendu syndrome

Definition

It is a familial syndrome characterized by the presence of multiple superficial telangiectasias (skin, lips, oral cavity, fingers, nasopharynx, and conjunctiva) combined with arteriovenous malformations (AVMs) of the internal organs (lung, brain, gastrointestinal tract, liver, and spinal cord) (Goldberg and Bullock 1990; Ferri et al. 2014).

Etiology

HHT is a rare autosomal dominant disorder that leads to dysplasia of blood vessels throughout the body (Goldberg and Bullock 1990; Ferri et al. 2014). Gene mutations lead to endothelial cell loss and weakness in the perivascular connective tissue with subsequent dilatation of the vessel wall. Most commonly, HHT patients have mutations in the endoglin and activin A receptor-like kinase 1 (ALK1) genes. Endoglin, SMAD4, and ALK1 are involved in cell surface signaling via the transforming growth factor-β (TGF-β) receptor complex (Morelli 2011; Rinaldi et al. 2011).

Type	Gene with associated mutation
HHT type I	Endoglin
HHT type II	ALK1
HHT type III	Unknown
Juvenile polyposis and HHT (JPHT)	SMAD4

Clinical Presentation

Classically, patients present with recurrent epistaxis or gastrointestinal bleeds due to telangiectasias of the nasopharynx or AVMs in the GI system. Epistaxis is the most common clinical manifestation (90% of affected patients), followed by gastrointestinal bleeding (20–40%) and pulmonary arteriovenous malformations (15–20%) (Morelli 2011; Rinaldi et al. 2011). This autosomal dominant disease produces a syndrome of multiple orocutaneous telangiectasias, especially on the face, lips, tongue, oral mucosa, conjunctiva, retina, and choroid, with associated internal AVMs. The cutaneous or mucosal lesions are typically bright red, non-pulsatile, and blanch under direct pressure.

Ocular symptoms are rarely the basis for the patient presentation to the ophthalmologist office. Patients can present with recurrent subconjunctival hemorrhages, bloody tears, conjunctival vascular tumors, or decreased vision secondary to macular edema as a result of a retinal vein occlusion, generalized retinopathy, or leaking retinal or choroidal telangiectasias in and around the macula (Goldberg and Bullock 1990; Morelli 2011; Rinaldi et al. 2011; Ferri et al. 2014).

Diagnosis

Curaçao Criteria:

- Spontaneous recurrent epistaxis
- Multiple telangiectasias (face, mouth, lips)
- Internal arteriovenous malformations
- First-degree relative with HHT

Diagnosis is defined by the presence of three criteria; two criteria give a possible diagnosis; and less than two criteria make the diagnosis unlikely (Rinaldi et al. 2011).

Differential Diagnosis

1. Recurrent subconjunctival hemorrhages
   (a) Conjunctival tumors
   (b) Amyloidosis
2. Conjunctival telangiectasia
   (a) Age-related vascular changes
   (b) Vascular arteriovenous malformations (AVMs)
   (c) Ataxia telangiectasia
3. Bloody tears
   (a) Lacrimal sac tumors or stones
   (b) Conjunctival inflammatory lesions (pyogenic granuloma)
   (c) Conjunctival/corneal tumors

Prophylaxis

Surveillance monitoring of ferritin levels and CBC to monitor for occult bleeds. These patients should be followed closely by their internists to monitor their AVMs, as they may increase in number and size as the patient ages.

Therapy

Therapy is targeted at leaking retinal or choroidal telangiectasia if vision is affected. Caution with intraocular surgery as these patients may have a higher risk of choroidal hemorrhage.

Prognosis

Patient's lifetime prognosis depends on the severity of vascular dysplasia. Visual prognosis depends on the extent of retinal and choroidal vascular abnormalities. If there is no retinal vessel dysplasia, visual acuity will remain normal.

Epidemiology

The incidence is estimated to be between 1 in 8,000 and 1 in 16,500 (Ferri et al. 2014). Approximately 1.2 million people suffer from HHT (Ferri et al. 2014). The frequency is equal between male and female.

Cross-References

► Osler-Weber-Rendu Syndrome

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Hereditary Macular Dystrophy

► Macular Dystrophy

Hereditary Motor-Sensory Neuropathy Retinal Degeneration

► Charcot-Marie-Tooth Disease, Retinal Degeneration

Hereditary Progressive Arthro-Ophthalmopathy

► Stickler Syndrome (Hereditary Progressive Arthro-Ophthalmopathy)

Hereditary Recurrent Corneal Erosion

► Recurrent Corneal Erosion

Hereditary Sensory and Autonomic Neuropathy

► Hereditary Sensory Neuropathy, Neurotrophic Keratopathy

Hereditary Sensory and Autonomic Neuropathy (HSAN) III

► Riley-Day Syndrome (Familial Dysautonomia)

Hereditary Sensory Neuropathy, Neurotrophic Keratopathy

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Synonyms

Hereditary sensory and autonomic neuropathy

Definition

Collection of similar but distinct inherited neurodegenerative conditions characterized by progressive loss of peripheral sensation.

Etiology

Hereditary sensory neuropathies (HSNs), or hereditary sensory autonomic neuropathies (HSANs), arise from any of several mutations in several distinct genes. To date they are classified into five main subtypes (HSN/HSAN types I–V):

1. HSAN I

   The first and most common group of HSNs is characterized by autosomal dominant mutations of either the *SPTLC1* (serine palmitoyltransferase long-chain subunit 1) or the *RAB7* (a late endosomal GTPase protein) genes (Klein and Dyck 2005). The *SPTLC1* gene encodes a subunit of serine palmitoyltransferase (SPT), an important enzyme for the production of certain fats called sphingolipids. The mutations of this gene make SPT with reduced function, leading to a decrease in sphingolipids. Sphingolipids are found in myelin, and this decrease in sphingolipids disrupts myelin formation, resulting in loss of efficiency of nerve cells and eventually cell death (Klein and Dyck 2005). The RAB7 protein is a small GTPase late endosomal protein involved in axonal vesicular transport. The mutations of the *RAB7* gene negatively affect retrograde tubular extensions, resulting in axonal atrophy and degeneration (Klein and Dyck 2005). The net effect of reduced myelinated fibers and axonal degradation is loss of sensory neural signal transmission and reduced motor neuron signal transmission, typically manifesting in loss of pain sensation in the distal parts of the lower limbs. The onset of these symptomatic deficits ranges from the second decade to fifth decade (Katirji and Koontz 2012).
2. HSAN II, Congenital sensory neuropathy

   HSAN II is an autosomal recessive disorder that has been linked to its own tentative *HSN2* gene located on chromosome 12 (Klein and Dyck 2005). Current research suggests a role for this HSN2 protein in nerve growth. The mutation of this gene is phenotypically characterized by marked demyelination as well as loss of unmyelinated fibers, causing lack of sensation and chronic ulcerations in the upper and lower extremities. The onset of HSAN II is in infancy or early childhood (Siddique et al. 2007).
3. HSAN III, Familial dysautonomia

   Familial dysautonomia, one of the more common forms of autosomal recessive HSAN, is most prevalent in Jewish infants and children and has been linked to the *IKBKAP* gene on chromosome 9 (Klein and Dyck 2005). The mutations on this gene have been found to disrupt production of a functional IKAP protein. Although the exact mechanism through which these mutations cause sensory neuropathy in the effected population is not known, inhibited development and maintenance of neuronal cells have been implicated in the neuropathologic progression of the disorder (Siddique et al. 2007). It is also characterized by autonomic dysfunction, hindered physical development, and reduction or the absence of sympathetic nerve endings (Klein and Dyck 2005). The disorder has a typical onset in infancy, often with premature death during infancy or childhood (Katirji and Koontz 2012).

4. HSAN IV, Congenital insensitivity to pain with anhidrosis

   HSAN IV, or the disorder commonly known as congenital insensitivity to pain with anhidrosis, is an autosomal recessive disorder linked to the *TRKA* gene (chromosome 1, encoding the TrkA protein), which is believed to be important for neurite outgrowth and development of embryonic sympathetic and sensory neurons (Klein and Dyck 2005). The mechanism of action of the TrkA protein, a transmembrane tyrosine kinase, is through the signal transduction of nerve growth factor (NGF). Defects in this protein appear to cause an absence of unmyelinated fibers, including those to sweat glands, causing anhidrosis (Pina-Garza 2013). The disorder has onset at infancy (Katirji and Koontz 2012).
5. HSAN V, Congenital insensitivity to pain with partial anhidrosis

   HSAN V shares many features of HSAN IV including congenital insensitivity to pain as well as partial anhidrosis. It has recently been declared its own category due to its selective reduction in unmyelinated nerve fibers, unlike in HSAN IV, which is characterized by the absence of these fibers (Katirji and Koontz et al. 2012). HSAN V is linked to mutations on the *NGFB* (for nerve growth factor-β) and *TRKA* genes, both of which are implicated in the development and maintenance of sensory neurons (Klein and Dyck 2005). NGF-β protein is a signaling molecule that binds to TrkA during development in order to promote differentiation and survival of nerve cells, the lack of which could explain disruption of proper sensory neuron innervation and insensitivity to pain in people with HSAN V (Siddique et al. 2007).

Clinical Presentation

The symptoms of the hereditary sensory neuropathies can be characterized into two broad groups of autosomal dominant (HSAN I) and autosomal recessive (HSAN II–V) disorders.

Dominant: The clinical onset for HSAN I is typically the second or later decades, manifesting initially as diminished sensation in the distal portions of the lower limbs with progressive degeneration over time (Lloyd and Chaudhry 2011). Some patients experience spontaneous pain from these regions, including lancinating or burning pain from the feet, which is exacerbated by excessive use. The characteristic loss of sensation from the distal lower limbs eventually causes loss of pain and temperature sensation, leading to a variety of complications in these areas (Katirji and Koontz 2012). Common features include deep foot ulcerations, cellulitis, osteomyelitis, and foot bone resorption (Klein and Dyck 2005).

Recessive: The clinical features of autosomal recessive HSAN (II–V) disorders typically present in infancy or early childhood (Siddique et al. 2007). Similar loss of sensory modality as in the autosomal dominant disorders is found in the distal parts of both the upper and lower limbs, as well as in the trunk. There is often complete loss or depression of tendon reflexes in all limbs (Klein and Dyck 2005). In conjunction with loss of neuropathic joint degeneration, the loss of pain and temperature sensation often leads to complications such as ulcerations, bone fractures, infections, and bone resorption in all the distal limbs (Pina-Garza 2013). Patients may also exhibit autosomal dysfunction such as anhidrosis. This can also cause a cohort of problems affecting gastrointestinal function in the form of abnormal esophageal peristalsis, oropharyngeal incoordination, gastroesophageal reflux, and chronic lung disease (Klein and Dyck 2005). In addition, the combination of dysautonomic functions such as alacrima with corneal insensitivity from peripheral sensory deficits predisposes HSAN patients to ulceration and scarring of the cornea or neurotrophic keratopathy (Katirji and Koontz 2012). Other features of more severely affected patients with congenital HSANs include mental retardation and premature death (Klein and Dyck 2005).

Diagnosis

The diagnosis of HSAN involves both the recognition and the degree of sensory and autonomic

dysfunction in patients. All the HSAN disorder types show complete penetrance, but exhibit wide variability in terms of their clinical presentation. A simple way to test sensory axonal neuropathy is via the histamine test to examine axonal integrity (Katirji and Koontz 2012). A lack of normal axon flare response to intradermal histamine injection can suggest deterioration of unmyelinated C-fibers, a characteristic common to most HSAN patients. Other sensory and autonomic deficits in patients can be matched to the constellation of clinical features of each HSAN type for diagnosis. Genetic testing for known genes should be administered to establish a more definitive diagnosis whenever possible (Klein and Dyck 2005).

Differential Diagnosis

Electrodiagnostic testing of sensory nerves, glucose tolerance test, and laboratory testing can help to differentiate HSAN from other sensory neuropathies (Lloyd and Chaudhry 2011). Charcot-Marie-Tooth (CMT) disease may closely resemble HSAN, yet HSAN patients typically present with more severe sensory deficits and less motor deficits than CMT patients (Katirji and Koontz 2012). Sudomotor testing and skin biopsy can further confirm autonomic and small-fiber sensory involvement, respectively, while amyloidosis and vasculitis can be excluded via nerve biopsy (Lloyd and Chaudhry 2011).

Prophylaxis

Genetic counseling of at-risk family members of HSAN patients should be implemented. Patients should maintain constant vigilance in order to minimize injuries to peripheral limbs, skin, and bones.

Therapy

There is currently no gene therapy or treatment available for any of the known HSAN types. The goal of the therapy for HSAN, therefore, remains symptomatic and geared toward the prevention of self-mutilation to avoid the development of debilitating deformities such as ulcers and stress fractures in the upper and lower limbs (Klein and Dyck 2005). Patients should be carefully inspected daily for injuries to hands and feet. Early recognition and proper use of antiseptic techniques may help prevent osteomyelitis and amputations. Sharp pains can be partially relieved through careful selection of drugs, such as certain combinations of antiepileptics and antidepressants. For autosomal recessive HSAN subtypes (HSAN II–V), which show infantile onset, treatment of self-mutilation can also involve smoothing of teeth and early habit-reversal behavioral therapy for self-injurious behaviors (Lloyd and Chaudhry 2011).

Prognosis

The development of HSAN type I can be better managed given the later onset of symptoms with proper training and precautions to prevent self-mutilation. With the infantile onset of symptoms for affected individuals with the autosomal recessive disease, management of HSAN types II–V remains more difficult. Smoothing of teeth, habit-reversal behavioral therapy, and the use of braces have helped improve the outcome of patients (Lloyd and Chaudhry 2011).

Epidemiology

HSAN is a rare disease and its prevalence varies with each subtype. The lack of prospective epidemiologic studies makes it difficult to determine the prevalence of the disease as a whole, although the gene frequency for the more common recessive form HSAN III (familial dysautonomia) has been estimated to be at 0.01 per 100,000 Jews in the United States (Siddique et al. 2007).

Cross-References

► Neurotrophic Keratopathy

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Herpes Simplex Stromal Keratitis

► Stromal Keratitis (Herpetic)

Herpes Simplex Virus

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Synonyms

HSV

Definition

Double-stranded DNA viruses with two closely related subtypes, HSV-1 and HSV-2.

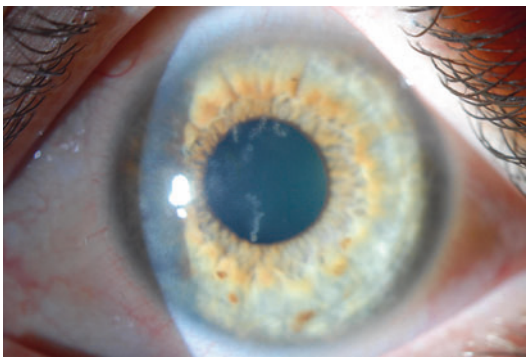
Etiology

Transmission occurs when live virus encounters exposed mucosal surfaces or skin breaks. Primary infection is often asymptomatic but may manifest as a mild fever and upper respiratory illness. HSV survives in a latent form in the central nervous system (CNS) of its host; HSV-1 most commonly resides in the trigeminal ganglia and causes ocular disease through reactivation.

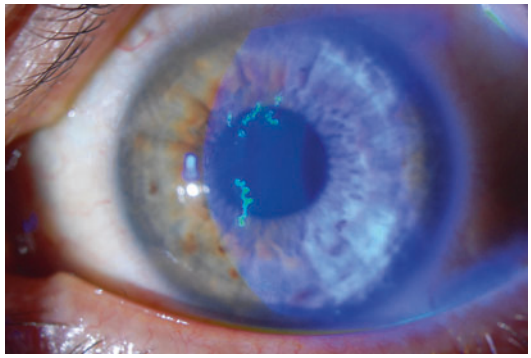
Clinical Presentation

Recurrent HSV has a predilection for the cornea. The most common manifestation is reduced corneal sensation and epithelial keratitis with a central, dendritic ulcer with terminal bulbs (Figs. 1 and 2). Patients present with tearing, blurred vision, and mild irritation or foreign body sensation. Complications include secondary bacterial infection, neurotrophic keratopathy, and corneal scarring.

Less commonly, stromal disciform keratitis is present. Patients experience blurred vision and photophobia. Findings include a central zone of stromal and epithelial edema, folds in Descemet's membrane, and a ring of stromal haze resulting from deposition of viral antigen and immune complexes in the stroma. Associated findings may include anterior uveitis with endothelial keratic precipitates, increased intraocular pressure, and



Herpes Simplex Virus, Fig. 1 Slit lamp photograph demonstrating classic dendritic ulcer in a patient with corneal disease secondary to reactivation of HSV-1 (Courtesy of Dr. Christopher J. Rapuano, Wills Eye Institute)



Herpes Simplex Virus, Fig. 2 Photograph, with a cobalt blue filter in place, of the same ulcers stained with fluorescein (Courtesy of Dr. Christopher J. Rapuano, Wills Eye Institute)

corneal neovascularization or ghost vessels. Complications include corneal scarring, glaucoma, cataract, and iris atrophy.

Acute retinal necrosis (ARN) results from reactivation in the retina. It typically occurs in *immunocompetent* individuals. Findings include granulomatous anterior uveitis, occlusive retinal vasculitis involving arteries and veins, retinitis and retinal necrosis in the periphery with circumferential spread, vitritis, and optic neuropathy. Complications include retinal breaks, detachments, and proliferative vitreoretinopathy.

Diagnosis

The true dendritic ulcer is pathognomonic. HSV may be isolated from corneal scrapings, cultured from corneal tissue, or identified by polymerase chain reaction performed on samples of the tears, epithelium, or anterior chamber fluid. Serology is of limited use given the high prevalence of positivity in the general population.

Differential Diagnosis

The differential diagnosis of dendritic or disciform keratitis includes:

Herpes zoster keratitis
Healing corneal abrasion
Keratoconjunctivitis sicca
Acanthamoeba keratitis
Toxic keratopathies secondary to topical medication
Bacterial or fungal keratitis
Interstitial keratitis

ARN from HSV infection may mimic:

Behçet disease
Fungal endophthalmitis
Cytomegalovirus retinitis
Syphilis
Sarcoidosis
Toxoplasmosis
Retinitis associated with collagen vascular diseases (e.g., systemic lupus erythematosus)

Prophylaxis

Maintenance therapy with oral acyclovir or valacyclovir reduces recurrence, but this effect is lost when the medication is stopped.

Therapy

Treatment includes antivirals, often in combination with a topical steroid. Dendritic keratitis may be treated with topical antivirals like trifluridine or vidarabine. Systemic antivirals, such as acyclovir or valacyclovir, are as effective as topical formulations and avoid the corneal toxicity. Stromal keratitis is treated similarly. Topical antibiotic ointments may prevent secondary bacterial infection, especially when topical corticosteroids are employed. For ARN, inpatient admission with intravenous antivirals is usually indicated and helps prevent ARN in the fellow eye. In severe cases, systemic steroids may limit the damage from retinal inflammation. Performed after the acute infection, laser retinopexy may prevent detachments. Patients must be evaluated for CNS involvement including life-threatening herpetic encephalitis.

Prognosis

Dendritic keratitis usually heals with relatively little scarring. Complications result with repeated recurrences or in undiagnosed or ineffectively treated cases. Disciform keratitis usually has favorable resolution; if associated with stromal keratouveitis, the course is often prolonged and unpredictable with repeated scarring and vision loss. ARN carries a very poor visual prognosis.

Epidemiology

HSV-1 seropositivity increases with age; 80% are positive by age 60, and it is estimated that one-third of the world's population is afflicted with some form of recurrent HSV-1 infection.

Cross-References

- ▶ Acute Retinal Necrosis (Necrotizing Herpetic Retinitis)
- ▶ Disciform Keratitis, Herpes Simplex Virus Causing
- ▶ Human Herpes Virus
- ▶ Keratitis
- ▶ Neurotrophic Keratopathy
- ▶ Uveitis in Multiple Sclerosis

Further Reading

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Herpes Stromal Keratitis

▶ Nonnecrotizing Keratitis

Herpes Zoster

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Synonyms

Shingles; Zoster

Definition

Disease secondary to reinfection or reactivation of latent varicella zoster virus (VZV)

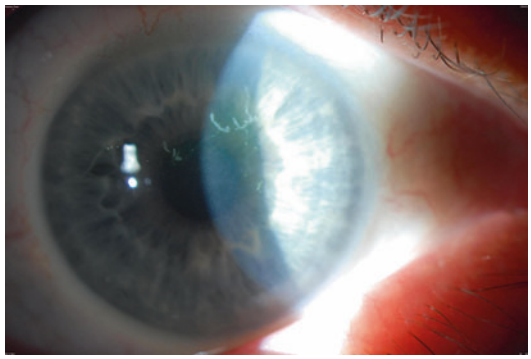
Etiology

VZV causes a primary infection (varicella, chickenpox); reactivation of latent virus in the neural ganglia causes herpes zoster (HZ), most commonly seen in older or immunocompromised patients. Subclinical reactivations and reinfections occur throughout life but are limited by VZV-specific cell-mediated immunity.

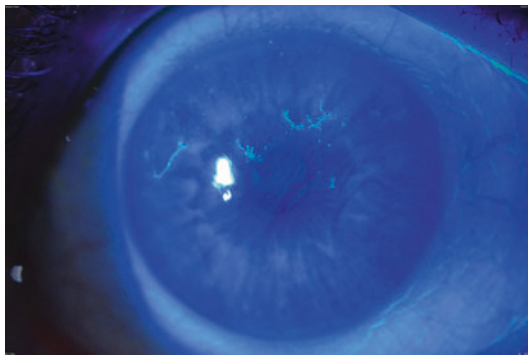
The pathophysiology of postherpetic neuralgia (PHN), persistent pain following HZ, remains unclear. It appears to be a disease of the CNS resulting in abnormal sensory processing and development of pain response to nonpainful stimuli.

Clinical Presentation

After a few days of fever, headache, malaise, and dysesthesia, a characteristic rash develops and involves one to three adjacent dermatomes of the



Herpes Zoster, Fig. 1 Slit lamp photograph demonstrating pseudodendritic lesion, without terminal end bulbs, in a patient with HZO (Courtesy of Dr. Christopher J. Rapuano, Wills Eye Institute)



Herpes Zoster, Fig. 2 Photograph, with a cobalt blue filter in place, of the same pseudodendrites stained with fluorescein (Courtesy of Dr. Christopher J. Rapuano, Wills Eye Institute)

affected ganglia. If an attack is limited, a rash might not develop (zoster sine herpete). More typically, grouped vesicles progress to pustules which may be hemorrhagic and crust after 7–10 days. Commonly affected dermatomes are those of the thorax (T3–L3) and those served by the trigeminal nerve. In herpes zoster ophthalmicus (HZO), damage from the infection or immune-mediated response can result in significant anterior or posterior segment complications (Figs. 1 and 2).

Viremia with dissemination (more than 20 pustules at sites nonadjacent to the primarily affected dermatomes) to cutaneous and extracutaneous sites is much more likely in immunocompromised patients who may develop visceral involvement of the lungs, liver, and brain. Neurologic complications of HZ include motor neuropathies, encephalitis, meningoencephalitis, myelitis, and Guillain-Barré syndrome. Of note, weeks to months after HZO, a cerebral vasculopathy with contralateral hemiparesis can occur and carries a mortality rate of 25%. The most common neurologic complication is PHN which can be particularly incapacitating.

Diagnosis

The characteristic pain and rash are usually sufficient for diagnosing HZ. Scrapings from a vesicle base can be sent for staining (Tzanck smear), cytology, PCR, or culture, and immunodiagnostic methods can confirm acute or recurrent VZV infection. Laboratory confirmation may help in unclear cases like zoster sine herpete. Although 90% of adults have detectable titers, only 5% without disease have titers of 1:640 or higher.

Differential Diagnosis

Herpes simplex virus (HSV).

Prophylaxis

Varicella virus vaccine is recommended for nonpregnant individuals aged 12 months or older without history of chickenpox or with negative serology. Theoretically, the vaccine could be used to prevent HZ by boosting immunity in patients who previously had varicella. HZ has occurred in vaccinees, especially those who had a rash. Unlike community-acquired infection with high levels of viremia and rash, vaccination usually produces little or no viremia. Thus, it is less likely for virus to become latent in the ganglia, and the incidence of HZ may decrease in the future. However, there is concern that initial vaccination may alter the epidemiology of HZ and, without widespread use, shift the prevalence of

varicella infection to an older population prone to complications not usually seen in children.

Therapy

If started within 72 h after the rash appears, antivirals such as acyclovir, valacyclovir, and famciclovir may limit viral replication, accelerate healing, and decrease the early pain of HZ. However, long-term (beyond 6 months) reduction in PHN has not been proven. Aggressive pain control and antidepressants such as amitriptyline or nortriptyline in older patients may reduce PHN by modifying the CNS effect. Topical agents like capsaicin cream may be of some benefit, but studies are inconclusive since the cream itself causes burning. Referral to a pain management clinic may be useful.

Steroids may improve the quality of life in the early stages but appear to have no long-term effect on PHN in HZ. Their judicious use, along with antivirals in older patients with moderate to severe pain and without contraindications, remains controversial in HZ. However, in HZO, carefully monitored use of steroids may reduce the complications from the inflammatory response. Current recommendations for acute HZO include antiviral, steroids, antidepressant, and pain medication.

HZ in patients younger than 45 years of age should trigger an investigation for HIV or other causes of impaired immunity. Immunocompromised patients must be treated with intravenous antivirals and monitored closely; they have a significantly increased risk of disseminated disease and poorer prognosis.

Prognosis

The major predictor of the severity of infection is the ability of the immune response to limit spread of the virus. The course is more severe and prolonged in immunosuppressed patients who also have an increased risk of dissemination.

If the side of the tip of the nose is involved, 50–85% of patients develop ocular complications, but roughly half of patients without Hutchinson's sign also have serious ocular involvement.

Increased age and prodromal symptoms are associated with increased PHN. PHN also appears to be increased in HZO compared to HZ elsewhere.

Epidemiology

HZ occurs in 20% of infected individuals with trigeminal nerve involvement in approximately 15% of cases. Incidence increases with age and immunosuppression.

Cross-References

- ▶ Herpes Zoster Ophthalmicus
- ▶ Human Herpes Virus
- ▶ Hutchinson-Tay Choroiditis
- ▶ Postherpetic Neuralgia
- ▶ Varicella Zoster Virus

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Herpes Zoster Ophthalmicus

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Synonyms

Varicella zoster virus

Definition

Herpes zoster ophthalmicus (HZO) is a recurrent infection with varicella zoster virus (VZV) affecting the first division of the trigeminal nerve.

Etiology

Herpes zoster infection may result from reactivation of a latent virus in the sensory ganglion or reinfection from contact with an exogenous viral source. The virus has an incubation period of a few days to 2 weeks from the time of exposure (Pavan-Langston 2005). In HZO, the virus affects the ophthalmic division of the trigeminal nerve, which divides into the nasociliary, frontal, and lacrimal branches (Lee and Liesegang 2011). A depressed cell-mediated immune response, such as in the elderly, HIV-infected individuals, organ transplant recipients, and individuals with malignancies, increases the risk of herpes zoster development (Gerstenblith and Rabinowitz 2012).

Clinical Presentation

Dermal, Extraocular Muscle, and Orbital Involvement

Herpes zoster ophthalmicus may present initially with a prodrome of headache, fever, malaise, blurred vision, eye pain, and red eye. The prodrome is followed by dermatomal pain and paresthesias 24–48 h later. The affected dermatome in herpes zoster ophthalmicus is the first division of the fifth cranial nerve. Hyperemic, hyperesthetic edema of the involved dermatome develops 2–3 days later, which develops into a skin rash. The rash initially develops as a macular rash, which becomes papular and then vesicular within 24 h. These vesicles continue to form for the following 3–5 days. Over the next 2–3 weeks, the vesicles become turbid and crust over, usually forming hemorrhagic scabs. In immunocompromised individuals, the vesicles may persist for weeks (Lee and Liesegang 2011). Herpes zoster affects the epidermis through the corium and forms deep eschars that may leave residual pitting or permanent scars (Pavan-Langston 2005). The rash is characteristically unilateral and does not involve the lower eyelid. Involvement of the tip of the nose from the nasociliary branch of the trigeminal nerve is known as the Hutchinson sign. The Hutchinson sign predicts higher risk of ocular involvement. Less commonly, the maxillary and mandibular divisions of the trigeminal nerve may also be involved, affecting the lower eyelid, cheek, and jaw of the involved side (Gerstenblith and Rabinowitz 2012). Hematogenous spread of the virus may result in crops of vesicles in remote sites. Visceral dissemination commonly affects the lungs and gastrointestinal tract and can be a severe complication (Lee and Liesegang 2011).

HZV skin and ocular ulcerations may result in complications of ptosis, lid retraction, or sloughing of lashes and lid tissues. Lid changes secondary to HZO include trichiasis, ectropion, entropion, madarosis, or poliosis. Contraction of the eyelids may lead to chronic corneal exposure and scarring (Lee and Liesegang 2011). Cranial nerve III, IV, and VI palsies are not uncommon, but they tend to resolve completely regardless of initial severity. Other possible palsies secondary to HZV include internuclear ophthalmoplegia, isolated iris sphincter paralysis, and Horner's syndrome. The associated palsies and orbital edema may be due to perineuritis and perivasculitis from generalized orbit inflammation. Most palsies will resolve spontaneously. Acute dacryoadenitis may develop, presenting with severe ocular pain and red eye. Elderly and immunocompromised individuals are at risk of developing superior orbital syndrome with complicating meningoencephalitis (Pavan-Langston 2005).

Conjunctivitis

Herpes zoster ophthalmicus can affect virtually any ocular structure. Ocular inflammation may present during acutely or months later, and become recurring. Conjunctivitis may present as a watery follicular reaction with or without petechial reaction and regional adenopathy. It may also present as a necrotizing membranous inflammation (Pavan-Langston 2005). A vesicular eruption can occur on the conjunctiva, leading to

rupture and possible hemorrhagic changes of the tissue. Severe conjunctival changes can lead to conjunctival scarring and symblepharon formation (Lee and Liesegang 2011). Conjunctival changes can spread to the puncta, leading to scarring, punctal occlusion, and epiphora (Lee and Liesegang 2011).

Episcleritis and Scleritis

Episcleritis or a scleritis can manifest acutely or even months later after resolution of the zoster vesicles. Episcleritis is typically seen early in the disease course, but it is not uncommon for it to persist for up to and beyond 3 months (Lee and Liesegang 2011). Scleritis that is flat and diffuse or focal with nodular elevations is a common finding in HZO. The nodular form of scleritis may lead to scleral thinning and staphyloma formation (Pavan-Langston 2005). Scleritis has a tendency to progress toward the perilimbal region of the cornea, which can result in a peripheral limbal vasculitis. Sclerokeratitis usually develops approximately 1 month after HZO onset (Lee and Liesegang 2011).

Keratitis and Pseudodendrites

Corneal disease may follow several days to months after the acute rash presentation and may last for years. Corneal manifestations of herpes zoster ophthalmicus may present as diffuse superficial punctate keratitis or multiple small migratory epithelial dendritiform lesions in the initial stages. Larger pseudodendrites, presenting as raised mucus plaques on the cornea or conjunctiva, SPK, immune stromal keratitis, and neurotrophic keratitis will follow (Gerstenblith and Rabinowitz 2012). VZV DNA shedding duration is highly variable, age dependent, and may relate to immune status (Pavan-Langston 2005).

Corneal zoster involvement presents initially as coarse punctate epithelial keratitis with blotchy, swollen, epithelial cells. They are usually multiple, small, raised, and focally located along the periphery, and they can be stained with rose Bengal stain. Within a few days, multiple dendritic or stellate lesions of the involved epithelial cells develop, and they are typically found along the periphery of the cornea. They can be differentiated from herpes simplex associated dendrites by their superficial involvement, blunt dendrites, lack of central ulceration, and minimal staining with fluorescein and rose Bengal (Lee and Liesegang 2011).

Stromal Immune Disease

Anterior stromal infiltrates may develop as isolated or multiple patches of hazy, granular, dry infiltrates under the Bowman's layer, usually appearing 10 days after the onset of disease. The infiltrates typically underlie previous epithelial lesions. They may represent stromal reaction to viral antigen or direct viral cytotoxicity (Lee and Liesegang 2011). Other immune reactions that may develop include necrotizing interstitial keratitis with neovascularization, Wessely rings, or limbal vasculitis. When interstitial keratitis is associated with herpes zoster infection, there is increased risk of deep neovascularization with lipid deposition and fibrovascular scarring (Pavan-Langston 2005).

Keratouveitis and Endotheliitis

One week into the disease course, sudden onset of Descemet's folds and subsequent epithelial and stromal edema may develop. The folds may be localized or diffuse with underlying keratic precipitates and associated uveitis. This reaction may be due to direct viral invasion of the endothelium. The immune reaction may be manifest as a mild disciform keratitis or as a severe granulomatous inflammatory reaction (Lee and Liesegang 2011).

Corneal Mucus Plaques

Corneal mucus plaques typically develop months after acute HZO in a quiescent or minimally smoldering eye. They develop suddenly as coarse gray-white branching elevated lesions on the surface of edematous epithelial cells. They have sharp margins and lack terminal branches. They tend to stain well with rose Bengal but minimally with fluorescein. Mucus plaques vary in size and are migratory in nature. The etiology is unclear but may represent an immune reaction or result from mechanical causes, such as neurotrophic changes or an abnormal epithelial receptor site. VZV viral DNA has been detected within the

lesions by polymerase chain reaction (PCR), which may suggest an infectious etiology (Lee and Liesegang 2011).

Disciform Keratitis

Disciform keratitis presents weeks to months after acute HZO. It appears as a deep central or peripheral disk-shaped area of stromal edema. There are typically minimal infiltrates and the epithelium remains intact. A relatively quiescent eye may show multiple sites of corneal edema. Disciform keratitis of HZO may be associated with immune rings, most commonly seen in the central or paracentral cornea (Lee and Liesegang 2011).

Neuroparalytic Keratopathy and Neurotrophic Ulcers

Herpes zoster keratitis may result in markedly diminished corneal sensation, with 60% of patients experiencing moderate to complete corneal anesthesia (Pavan-Langston 2005). Diminished corneal sensation resolves in most, though some may never regain normal sensation. Approximately 20% of patients are estimated to have decreased corneal sensitivity at 1 year after onset of HZO (Lee and Liesegang 2011). The more intact the corneal sensation the better the prognosis for the cornea. The neuroparalysis of herpes zoster develops secondary to the destructive VZV ganglionitis and aqueous tear deficiency due to loss of the nasolacrimal reflex. Corneal anesthesia may develop with the acute illness or over the next 2–3 weeks. One of the most dangerous forms of herpes zoster keratitis is anesthetic epithelial breakdown due to permanent corneal anesthesia. One fourth of patients with HZO develop clinical signs of neurotrophic keratitis, which may begin as a dull or irregular corneal surface with mild punctate epithelial keratitis. Diffuse epithelial edema or haze with fine intraepithelial vesicles may follow. Reduced blink frequency and an unstable tear film further aggravate this condition. Oval epithelial defects may develop in the palpebral fissure or lower corneal region, which progress to corneal melting and subsequent thinning (Pavan-Langston 2005). Complications, such as superinfection, corneal thinning, corneal perforation, and fibrovascular scarring, may occur and suggest a worse prognosis (Lee and Liesegang 2011).

Iridocyclitis

Frequency of anterior uveal tract involvement is second only to the cornea. Involvement may present acutely, months later, or both. Symptoms include pain, decreased vision, and photophobia. Patient may have signs of ciliary hyperemia, keratic precipitates, and iris edema. Anterior peripheral and posterior synechia formation with a fibrinous exudate may be present in more severe cases. Herpes zoster iritis develops from a diffuse infiltrate of the iris stroma. Striate keratopathy, vascular dilation, sphincter damage, and sectoral iris atrophy have been characterized in herpes zoster ophthalmicus. Occlusion of iris vessels at the sites of iris atrophy has been noted by fluorescein angiography (Pavan-Langston 2005). Ischemic occlusive vasculitis associated with ciliary body inflammation, segmental iris distortion, and sectoral iris atrophy may be the cause of zoster iritis (Lee and Liesegang 2011).

Up to 40% of patients with HZO develop anterior uveitis. The inflammation may be granulomatous or nongranulomatous, and it is usually associated with keratic precipitates and corneal edema. Less commonly, the uveitis of HZO may occur independent of corneal involvement (Lee and Liesegang 2011). Zoster iritis may lead to development of a hypopyon, hyphema, heterochromia iridis, sympathetic ophthalmia, hypotony, and phthisis. Herpes zoster associated uveitis may result from an immune reaction to the antigenic residua of the virus or to new virus production. Twenty-five percent of patients with VZV uveitis progress to develop posterior pole complications. These complications include cystoid macular edema, epiretinal membranes, papillitis, and retinal fibrosis and detachment (Pavan-Langston 2005). In a retrospective study, secondary glaucoma developed in 56% of patients with HZO associated uveitis (Lee and Liesegang 2011).

Glaucoma

HZO may cause an imbalance between the decreased aqueous production and outflow

blockage by these mechanisms, leading to intraocular pressures ranging from abnormally low to severe secondary glaucoma. The alteration may result from extension of VZV to the trabecular meshwork or a severe ischemic vasculitis (Lee and Liesegang 2011). Elevated intraocular pressure secondary to herpes zoster ophthalmicus may be acute or transient, or it may become a chronic problem. Glaucoma is the most common secondary complication of VZV uveitis (Pavan-Langston 2005). The inflammatory glaucoma associated with HZO uveitis may result from multiple mechanisms. The trabecular meshwork may be blocked by cellular debris, iris pigment, or blood. Peripheral anterior synechiae may interfere with aqueous fluid drainage. Posterior synechiae may cause a pupillary block. Additionally, the trabecular meshwork may undergo structural changes (Lee and Liesegang 2011).

Acute Postherpetic Neuralgia and Postherpetic Itch

Though the skin rash of herpes zoster ophthalmicus usually resolves within 2–3 weeks, patients may be troubled by persistent pain in the involved dermatome. Herpes zoster ophthalmicus may manifest with multiple different types of pain or discomfort. Postherpetic neuralgia may cause a constant aching or burning pain, a sudden lancinating pain, or nonpainful stimuli may be perceived as painful. Postherpetic itch is a constant or intermittent itching in the involved area. These conditions may manifest as sleep disturbances, anorexia, constipation, and depression. Maximal recovery is typically achieved by 2 years after the acute illness. The initial pain of herpetic neuralgia has been attributed to acute swelling of the trigeminal neuralgia associated with a neural vasculitis, nerve and axon necrosis, focal hemorrhage, and periocular tissue inflammation. Cases of severe pain may have associated sympathetic hyperactivity, including tachypnea, tachycardia, diaphoresis, and mydriasis (Pavan-Langston 2005).

Zoster Sine Herpete

Zoster sine herpete (ZSH) is a reactivated VZV infection that causes only neurologic symptoms, including dermatomal neuralgia or neuropathy, and occasional ocular inflammation. By definition, ZSH does not cause a rash. A facial palsy (Bell's palsy), granulomatous iritis, and disciform keratitis may develop as a result of ZSH (Pavan-Langston 2005).

Diagnosis

The diagnosis of herpes zoster ophthalmicus is made by clinical impression based upon the characteristic signs and symptoms of the infection. However, herpes zoster can mimic other diseases, such as herpes simplex and impetigo, so laboratory testing is needed on occasion. These tests include morphologic and immunomorphologic tests, viral isolation, serologic tests, and cellular immunity tests (Lee and Liesegang 2011).

The simplest morphologic test is the Tzanck smear, which can identify a herpes virus but cannot distinguish it from the various different types of herpes viruses. Various stains can be used to confirm the presence of multinucleated giant cells and the characteristic acidophilic intranuclear inclusions in epithelial cell scrapings. These stains include hematoxylin & eosin, Giemsa, Papanicolaou, Wright, and toluidine blue (Lee and Liesegang 2011). Immunologic tests include immunofluorescent and immunoenzyme stains. Direct immunofluorescence assay can be used to confirm suspicion of herpes zoster infection as it is sensitive and specific with the benefit of lower cost and rapid execution time (Pavan-Langston 2005). Polymerase chain reaction (PCR) technique is rapid and very sensitive, but it is difficult to distinguish between active disease, inactive viral particles, and recurrent disease with this test (Lee and Liesegang 2011).

The definitive technique for VZV identification is by culture of vesicular fluid. The virus can be cultured from skin vesicles and ocular lesions for up to 7 days after their appearance in an immunocompetent individual and longer in an immunocompromised patient. However, culture growth of the virus is slow. Varicella zoster virus titers will rise after a zoster infection. Serologic evaluations include a number of different assays to measure

anti-VZV antibodies for indication of prior or recurrent infections. Serologic assays include fluorescent antibody staining for membrane antigen, immune adherence hemagglutination assay, passive hemagglutination, immunofluorescence, complement fixation, radioimmunoassay, immunoblot, and enzyme-linked immunosorbent assay (ELISA). HIV serologic testing should be considered in individuals less than 50 years of age who develop herpes zoster infection as HIV-positive individuals can be asymptomatic (Pavan-Langston 2005).

Differential Diagnosis

The differential diagnosis should include herpes simplex virus. The two can be distinguished by their regional involvement. The rash of herpes simplex virus is not dermatomal and crosses the midline. It typically affects young individuals (Gerstenblith and Rabinowitz 2012).

Herpes zoster ophthalmicus may closely mimic varicella zoster dermatitis. In severe cases, skin and periocular involvement may resemble bacterial orbital cellulitis (Pavan-Langston 2005).

Prophylaxis

A high-potency live attenuated Oka/Merck VZV vaccine was approved by the US FDA in 2006 for the prevention of herpes zoster in immunocompetent individuals 60 years of age or older. The shingles prevention study found that the vaccine reduced the overall incidence of herpes zoster by 51%. It also found that the vaccine reduced the burden of illness by 61% and the incidence of postherpetic neuralgia by 66%. It is estimated that the vaccine will effectively prevent 250,000 cases of herpes zoster in the USA each year. Studies are underway to determine the effectiveness of the vaccine in immunocompromised individuals. It is not yet known what the duration of the vaccine's protective effect is and whether a booster vaccine will be necessary to maintain the vaccine's efficacy (Lee and Liesegang 2011).

Therapy

Medical Treatment

Treatment of VZV is mainly supportive, treating the symptoms of the infection. Therapy includes hydration, nonaspirin antipyretics, cool baths, and careful hygiene to prevent superinfection of the skin lesions. Antiviral agents may be used in treatment. Acyclovir, valacyclovir, and famciclovir are FDA-approved for herpes zoster, and they are guanosine analogs that interfere with viral replication. A systemic review of 12 randomized controlled trials concluded that valacyclovir and famciclovir therapy has resulted in significant reduction in the risk of pain associated with HZO and should be the preferred therapeutic drugs given their efficacy in pain control and convenient dosing regimen (McDonald et al. 2012). Immunocompromised individuals may require intravenous acyclovir to prevent or treat the complications of disseminated disease. Oral acyclovir shortens the duration of the disease. Antivirals accelerate cutaneous lesion healing and decrease new lesion formation. However, controversy exists with regards to the use of oral antiviral drugs for localized zoster. Zoster immune globulin is not effective once the disease is contracted. However, it may confer passive immunity within 96 h of exposure in individuals at risk for severe infection (Lee and Liesegang 2011). Characteristics of patients at increased risk of complications include prematurity, age over 50 years, immunocompromise, severe pain at presentation, and increased area of skin involvement (Pavan-Langston 2005). Topical acyclovir was found to be effective in controlling herpes zoster keratouveitis compared to steroids, resulting in fewer recurrences and shorter recovery times. Shorter disease durations and decreased recurrence rates would likely result in decreased incidence of ocular damage and visual loss. The combination of acyclovir and steroids has been shown to result in prolonged treatment durations and higher recurrence rates (McGill et al. 1983)

Corticosteroids in combination with antivirals have been shown to have a moderate but statistically significant acceleration in cutaneous healing and acute pain alleviation than antiviral drugs

alone. Corticosteroids have not been shown to have any benefit in postherpetic neuralgia (Lee and Liesegang 2011). Topical steroids are useful in treatment of zoster vasculitis manifestations, including scleritis, stromal keratitis, interstitial keratitis, and uveitis. Corticosteroids suppress nonspecific inflammation and immune-mediated diseases, including anterior stromal infiltrates, stromal disciform reaction, corneal mucous plaques, sclerokeratitis, serpiginous ulceration, and keratouveitis. The role of systemic corticosteroids in acute HZO is controversial. Given the well-known adverse side effect profile and risk of disseminated infectious disease, the use of systemic corticosteroids should be limited to immunocompetant, nondiabetic patients experiencing vasculitic complications of HZO, such as severe scleritis and uveitis (Pavan-Langston 2005).

Development of corneal ulcers may be prevented with adequate preservative-free lubrication, topical antibiotic prophylaxis, and lateral tarsorrhaphy. Lower punctal plugs may be used to increase natural lubrication. If these measures are unsuccessful and the corneal epithelium is at risk of a break or an ulcer develops, soft contact lenses with continued lubrication and antibiotic prophylaxis should be initiated. If the corneal ulcer begins to melt, cyanoacrylate gluing is indicated. Neovascularization should be allowed to occur as a component of the healing process (Pavan-Langston 2005).

Acute neuralgia typically responds moderately well to mild analgesics. Postherpetic neuralgia and itch have been shown to be prevented or greatly inhibited by treatment initiated at the onset of acute illness with a combination of an antiviral, such as famciclovir or valacyclovir, with a tricyclic antidepressant or anticonvulsant and strong analgesic (Pavan-Langston 2005). There is no data to suggest that any tricyclic antidepressant is more efficacious than another in pain management. Selection of a drug for postherpetic neuralgia treatment is made based upon each drug's individual side effect profile (Lee and Liesegang 2011). A combination of neuroleptic agents can be used as an alternative to tricyclic antidepressants, but patients should be monitored for side effects of tardive dyskinesia and other extrapyramidal reactions. Anticonvulsants, such as pregabalin, gabapentin, and zonisamide, are very effective at controlling postherpetic neuralgia as single agents. Tricyclic antidepressants and anticonvulsants can be combined in patients who don't respond to a single agent. If the combination is still not effective, slow-release opioids, such as oxycodone-SR, can be added or used as a single agent (Pavan-Langston 2005).

Topical capsaicin has been tried as a way of depleting substance P from the small sensory peripheral and central neurons involved in pain sensation. It has not been shown to be effective as a single agent but may have some benefit as an adjuvant treatment (Pavan-Langston 2005). A variety of topical compounded growth factors have been beneficial in epithelial healing of neurotrophic keratopathy, such as autologous serum, substance-P-derived peptide, and insulin-like growth factor (Lee and Liesegang 2011). Lidocaine skin patches can be applied to the forehead or scalp and have been effective in treating postherpetic neuralgia and postherpetic itching. Diphenhydramine has been effective in reducing symptoms of postherpetic itching in many patients (Pavan-Langston 2005).

Frontal and nasal nerve blocks are effective in cases of severe pain associated with acute HZO that is not controlled by other drugs. Bupivacaine, epinephrine, and clonidine are injected at the frontal and nasal branch levels of the ophthalmic nerve. The injections are typically effective for 5 days and can be repeated. A stellate ganglion block may be effective if given within 14 days of rash onset. The stellate ganglion block consists of a 1% lidocaine and 0.5% bupivacaine mixture injected at the C5-6 vertebrae level with the head extended (Pavan-Langston 2005).

Surgical Treatment

Surgery is most commonly indicated in HZO for exposure keratopathy and anesthetic cornea. Punctal plugs may be sufficient if lid closure is adequate but the tear meniscus is low. More severe forms of HZO may lead to significant scarring or partial destruction of the eyelid, leading to impairment of normal lid closure. In cases where the lid

tissue is intact, a lateral or medial and lateral tarsorrhaphy may be adequate to protect the globe. If lid tissue has been lost, plastic reconstruction may be indicated (Pavan-Langston 2005).

A partial tarsorrhaphy is indicated in partial or total corneal anesthesia where the epithelium is unhealthy or prone to recurrent breakdown. A therapeutic contact lens may be used in these cases with adequate lubrication. In cases where corneal melting occurs, the area should be sealed with cyanoacrylate glue, and a Plano T therapeutic lens should be inserted to cover the rough surface of the glue. Over time, the cornea heals under the glue, and the glue dislodges spontaneously. Adequate alternatives, though more extensive surgical procedures, include pulling down a conjunctival flap if it has not been too scarred by the disease, placing a conjunctival transplant from the contralateral eye, or placing an amniotic membrane transplant (Pavan-Langston 2005).

Keratoplasty may be successful in a cornea that has scarred but maintained a reasonable amount of sensation. Anesthetic eyes tend to heal poorly and transplanted eyes are prone to melting and superinfection, making them poor candidates for keratoplasty (Pavan-Langston 2005). Deep anterior lamellar keratoplasty (DALK), penetrating keratoplasty (PK), and prosthokeratoplasty may be done in cases of severe scarring (Lee and Liesegang 2011). If keratoplasty is performed, a lateral tarsorrhaphy should be done to protect the graft (Pavan-Langston 2005).

Prognosis

The presence of Hutchinson's sign is a poor prognostic indicator due to the increased risk of ocular complications secondary to the extensive intraocular innervations of the nasociliary branch. Ocular involvement has no known correlation with age, gender, or severity of the zoster associated skin rash. The disease may present with acute, chronic, or relapsing phases. The visual outcome is highly variable. However, the visual prognosis in immunocompromised individuals tends to be significantly worse (Lee and Liesegang 2011).

Epidemiology

The frequency of herpes zoster affecting the trigeminal nerve is 9–16% and involvement of the ophthalmic branch varies in frequency from 8% to 56%. Of individuals with herpes zoster of the ophthalmic division of the trigeminal nerve, approximately 50–72% will have involvement of ocular structures, develop chronic disease, and sustain moderate to severe vision loss (Pavan-Langston 2005).

Cross-References

- ▶ Fuchs Heterochromic Iridocyclitis, Glaucoma
- ▶ Herpes Simplex Virus
- ▶ Herpes Zoster
- ▶ Orbital Apex Syndrome in Neuro-Ophthalmology
- ▶ Other Uveitic Etiologies

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Herpesviridae

- ▶ Human Herpes Virus

Hertwig-Magendie Sign

► Alternating Skew Deviation
► Skew Deviation

Heterochromic Cyclitis Fuchs' Glaucoma

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Synonyms

Fuchs' uveitis syndrome (FUS) with secondary glaucoma

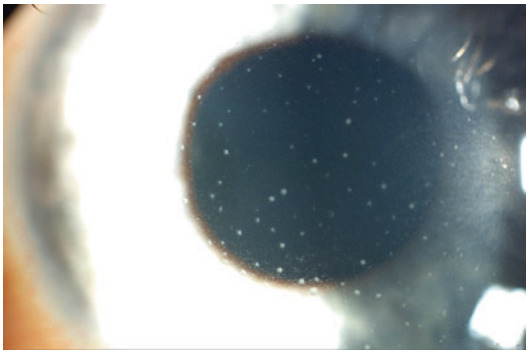
Definition

Intraocular pressure rise secondary to FUS leading to optic nerve damage

Etiology

Several, mostly infectious, causative agents have been discussed. In the last years, rubella came to the focus of attention as antibodies to rubella have been found in aqueous humor (Quentin and Reiber 2004), and an epidemiologic study showed a reduction of FUS since vaccination for rubella was introduced (Birnbaum et al. 2007). Mechanism of raised intraocular pressure (IOP) is thought to be mixed, on the one hand due to trabecular meshwork damage and thus increased outflow resistance due to the chronic inflammation and on the other hand by angle closure due to peripheral anterior synechiae or vascular membrane formation (Moura Filho and Liesegang 2010). Local corticosteroids may promote glaucoma.

Friederike Mackensen: deceased.



Heterochromic Cyclitis Fuchs' Glaucoma, Fig. 1

Clinical Presentation

The classic clinical phenotype of Fuchs' uveitis syndrome (FUS) is unilateral mild anterior to intermediate uveitis, no pain or redness, insidious onset (typically discovered when the patient attends to an eye care provider due to other reasons) with chronic course, responding little or not at all to topical corticosteroids, stellate or mixed (fine, small roundish, and stellate) keratic precipitates (KP) (see Fig. 1) in a diffuse distribution, in a young patient, diffuse iris transillumination defects and/or heterochromia, early cataract formation, whitish vitreous cell deposits, and lack of posterior synechiae or macular edema. Typical complications of FUS are cataract and glaucoma.

Diagnosis

The diagnosis is mainly a clinical one (see above). OCT can be used to exclude macular edema. Confocal microscopy can help detect low-grade stellate KP, and anterior chamber tap can show elevated antibodies to rubella to further confirm the diagnosis (Quentin and Reiber 2004; de Visser et al. 2008).

Differential Diagnosis

The differential diagnosis of FUS includes conditions with hypopigmentary heterochromia and raised IOP such as glaucomatocyclitic crisis and

herpetic uveitis or pigment dispersion syndrome. The iris atrophy of FUS can also help in differentiating it from other uveitis forms in which atrophy, if present, is associated with full-thickness sector atrophy. Anterior chamber tap can help to exclude infectious origins as herpetic virus.

Prophylaxis

Glaucoma is often resistant to treatment and should actively be screened for at least every 6 months in patients with Fuchs' uveitis syndrome. Local corticosteroids should be avoided as they show no effect and may promote glaucoma and cataract formation.

Therapy

No anti-inflammatory treatment is known to change the course of FUS. Local corticosteroids may only be warranted if used as a diagnostic means to differentiate from other uveitic forms. Medical and surgical treatment for reducing intraocular pressure should be especially aggressive in these patients. Compliance may be an issue. Cataract surgery and – if necessary for dense vitreous opacities – vitrectomy can be performed without immunosuppressive treatment.

Prognosis

Generally the prognosis depends on the development of glaucoma which is the most common cause of permanent vision loss in FUS patients. If glaucoma does not develop, vision can be reduced by cataract formation or dense vitreous opacities which can be removed surgically with near-normal operation risks.

Epidemiology

FUS is a rare entity found in about 7% of all patients and 11% of anterior uveitis patients in a tertiary care setting (Jakob et al. 2009). It is frequently first diagnosed in the second to third decade of life. In this cohort it was more frequent in male patients. Glaucoma can develop in 15–59% of cases. Cataract formation is frequent.

Cross-References

- ▶ Fuchs Heterochromic Iridocyclitis, Glaucoma
- ▶ Glaucoma Associated with Pigment Dispersion Syndrome (PDS)
- ▶ Posner-Schlossman Syndrome

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Hexagonal Keratotomy

- ▶ Astigmatic Keratotomy

HHV

- ▶ Human Herpes Virus

Hidradenoma, Clear Cell (Eccrine Acrospiroma)

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Synonyms

Adenoma of the clear cell type; Clear cell hidradenoma; Clear cell myoepithelioma; Cystic hidradenoma; Eccrine acrospiroma; Eccrine poroma; Eccrine sweat gland adenoma; Nodular cell hidradenoma; Porosyringoma

Definition

A solid cystic cutaneous nodule arising from the duct and secretory coil of eccrine sweat glands.

Etiology

Clear cell hidradenomas may be due to impaired drainage of eccrine sweat glands within the dermis.

Clinical Presentation

Flesh colored, solid or cystic intradermal nodules, typically 5–30 mm, covered by intact skin. Pressure applied to the lesion may produce tenderness in 20% of patients. They present in middle age and frequently occur on the head, but can occur anywhere on the body (Shields and Shields 1999; Albert and Jakobie 2008; Rabady et al. 2008).

Diagnostics

Excisional biopsy provides definitive diagnosis. Histopathologically, clear cell hidradenoma demonstrates a well circumscribed dermal lesion composed of lobules of epithelial cells in a biphasic pattern. The first layer is composed of round cells with clear cytoplasm, and the other layer is composed of spindle shaped cells with eosinophilic cytoplasm (Shields and Shields 1999; Albert and Jakobie 2008; Rabady et al. 2008).

Differential Diagnosis

Seborrheic Keratosis
Squamous Cell Carcinoma
Trichilemmoma

Prophylaxis

No preventative measures are known.

Therapy

Surgical excision provides definitive diagnosis. Solitary eccrine spiradenomas are typically benign. Multiple large eccrine spiradenomas may be treated with carbon dioxide laser.

Prognosis

Excellent. Malignant eccrine spiradenoma has been reported on the eyelids, and malignant eccrine porocarcinomas have been reported to metastasize to viscera, lymph nodes, and bone.

Epidemiology

Unknown.

Cross-References

► Eccrine Spiradenoma

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Hidrocystoma, Apocrine

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Synonyms

Apocrine cystadenoma; Cyst of Moll

Definition

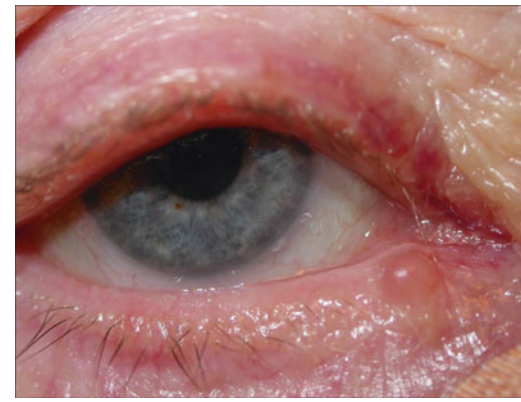
Benign cystic proliferations of the apocrine secretory glands (apocrine glands of the eyelids known as glands of Moll) (Nesi et al. 1998; Albert and Jakobiec 2008; Shields and Shields 2008).

Etiology

Unknown but blockage of the gland drainage ducts may lead to cyst formation.

Clinical Presentation

Usually appear as a solitary, soft, dome-shaped, slow growing papules or nodules with a cystic consistency, which can be translucent or frequently blue (Fig. 1). They are located most frequently on the eyelids margin, especially near the medial canthus.



Hidrocystoma, Apocrine, Fig. 1 Apocrine hidrocystoma on the right lower eyelid

Diagnostics

By typical clinical appearance; however, histologic examination often is required to establish a specific and definitive diagnosis.

Differential Diagnosis

Differential Diagnosis includes ► syringoma, ► blue nevus, eccrine hidrocystoma, ► basal cell carcinoma, ► malignant melanoma

Prophylaxis

Unknown.

Therapy

Surgical excision; remotion of the cyst wall is recommended to prevent recurrence. Multiple lesions can also be treated with trichloroacetic acid and CO_2 laser.

Prognosis

Benign lesions which are usually asymptomatic.

Epidemiology

Most lesions occur in adults or in the elderly; a few cases have been observed in both childhood and adolescence, both sexes are equally affected.

Cross-References

- ▶ Basal Cell Carcinoma of Eyelid
- ▶ Blue Nevus
- ▶ Malignant Melanoma (MM)

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Higher-Order Aberrations, Refractive Surgery

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Synonyms

Higher-order optical aberrations induced by refractive surgery

Definition

Monochromatic aberrations besides defocus and astigmatism that are induced by refractive-surgical procedures.

Basic Characteristics

With the opportunity of the measurement of the ocular wavefront error using wavefront sensors, it became obvious that refractive surgical procedures aiming at reducing ocular lower-order aberrations (LOA) also induce higher-order aberrations (HOA) (Applegate et al. 1996; Marcos et al. 2001; Bühren et al. 2004). While HOA in the normal human eye have a rather insignificant contribution to visual function, refractive surgery-induced HOA can lead to severe optical disturbances like haloes, ghost images, loss of contrast, and blurry vision (Chalita et al. 2004; Bühren et al. 2009a). Like in the normal eye, spherical aberration and coma are the dominant HOA, however, at significantly elevated levels. It has been shown that there is a linear relationship between the attempted spherical equivalent and the amount of spherical aberration (Marcos et al. 2001). The reason for the induction of HOA in LASIK is primarily the loss of laser fluence at the corneal periphery (Bühren et al. 2010) while coma is induced by decentration of the ablation (Bühren et al. 2010). Other reasons are the biomechanical response of the cornea to flap creation (Porter et al. 2003; Potgieter et al. 2005) and to incisions in radial keratotomy and implant surgery (Applegate et al. 1996; Bühren et al. 2004) as well as wound healing reactions (Bühren et al. 2009b). In current state-of-the-art refractive surgery novel technology such as aspheric ("wavefront-optimized") ablation profiles, the HOA induction can be efficiently minimized (Bühren et al. 2010).

In case of HOA-borne symptoms, the effect of HOA can be reduced by application of pupil-constricting eye drops such as pilocarpine or brimonidine (Bühren et al. 2005).

Cross-References

- ▶ Aberrometry
- ▶ Ametropia: Definition
- ▶ Comatic Aberrations

- ▶ Phakic IOL
- ▶ Radial Keratotomy
- ▶ Zernike Coefficients

References

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Higher-Order Optical Aberrations Induced by Refractive Surgery

- ▶ Higher-Order Aberrations, Refractive Surgery

High-Pressure Glaucoma

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Synonyms

Primary open-angle glaucoma (with elevated intraocular pressure)

Definition

High-pressure glaucoma is a subcategory of primary open-angle glaucoma with the adjunctive characteristic of elevated IOP.

Etiology

The main initializing event resides in the region of the trabecular meshwork, increasing aqueous outflow resistance and IOP.

Clinical Presentation

High-pressure glaucoma is usually insidious in onset, slowly progressive, and painless. Because central visual acuity is relatively unaffected until late in the disease, visual loss may be significant before symptoms are noted, especially in asymmetrical or unilateral cases.

Diagnosis

IOP $\geq$21 mmHg, optic nerve head with typical glaucomatous damage, visual field with progressive glaucomatous defects, wide open anterior chamber angle.

Differential Diagnosis

Other forms of elevated intraocular pressure combined with the typical features of ONH damage.

Therapy

The treatment is primarily medical with topical medications that reduce the aqueous humor production or facilitating its outflow. The inefficient reduction of the IOP requires a laser or an incisional surgical procedure such as laser trabeculoplasty, filtration surgery, insertion of aqueous drainage implants, or cyclodestructive procedures.

Prognosis

Most patients with POWG will retain useful vision for their entire lives. However, the incidence of blindness has been variously reported and has been estimated at 27% unilateral und 9% bilateral at 20 years following diagnosis in a certain population of patients. The age and severity at diagnosis are clearly important prognostic factors. Other prognostic factors are level of IOP, life expectance, family history, insufficient health care, decreased central corneal thickness, and myopia.

Epidemiology

Glaucoma is one of the leading causes of irreversible visual loss worldwide. The mean prevalence is estimated to be 1.96%. It has been estimated that by 2010, almost 45 million people will have open-angle glaucoma worldwide. Almost half (47%) of these people will reside in Asia, while 24% will be European. Individuals of African and Caribbean heritage have an increased risk of developing high-pressure glaucoma.

Cross-References

▶ Open-Angle Glaucomas
▶ Optic Neuropathy
▶ Uveitic Glaucoma

Further Reading

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High-Resolution Ultrasound Biomicroscopy

▶ Biomicroscopy, Ultrasound, of Anterior Segment

Hippel Disease

▶ Hemangioblastomas, with Retinal Angiomatosis (von Hippel Lindau Disease)
▶ Retinae (Retinal Angiomatosis, von Hippel Syndrome/Disease)
▶ VHL Syndrome

Hippel–Lindau Syndrome

▶ VHL Syndrome

Hippel–Lindau Syndrome, HLS

▶ Hemangioblastomas, with Retinal Angiomatosis (von Hippel Lindau Disease)
▶ Retinae (Retinal Angiomatosis, von Hippel Syndrome/Disease)

Histoacryl

▶ Cyanoacrylate Adhesive

Histoacryl Blue

▶ Cyanoacrylate Adhesive

HLS

▶ VHL Syndrome

Holmes-Adie Syndrome

▶ Tonic Pupil (Adie's Pupil), Pharmacological Testing for
▶ Anisocoria: Big Pupil
▶ Adie's Pupil (Tonic Pupil), Pharmacologic Testing

Holmium YAG Laser, Thermokeratoplasty

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Definitions

Thermokeratoplasty is the application of thermal energy to alter corneal curvature. This can be achieved by electrically heating a wire (conductive thermokeratoplasty) or via laser technology. Laser thermokeratoplasty (LTK) has the advantage of more targeted and controlled heat delivery, thereby avoiding spikes outside therapeutic temperature zones which cause necrosis, keratocyte damage, and increased wound-healing time. Numerous types of lasers for LTK have been explored, including carbon dioxide, hydrogen fluoride, erbium-glass, cobalt-magnesium fluoride, and, more notably, holmium:YAG (Ho:YAG) (Stasi and Azar 2007). Ho:YAG lasers are subcategorized as contact probe or noncontact type.

Indications

The idea of thermokeratoplasty has been described in literature dating back to 1879 with Gayet's use for keratoconus. Other reported applications include Lans in 1898 for corneal astigmatism, Terrien in 1900 for Terrien's marginal degeneration, O'Connor in 1933 for high myopic astigmatism, and Fyodorov of Moscow in 1981 for hyperopia (Stasi and Azar 2007). In modern refractive practice, the most established indication for holmium:YAG laser thermokeratoplasty (Ho:YAG LTK) by both the contact and noncontact types is mild to moderate hyperopia. Other indications described in literature include astigmatism associated with hyperopia and myopia. The use of LTK for myopia is still an ongoing investigation. LTK may be used to treat refractive error which is primary in nature as well as that induced by or residual from prior eye surgery (Eggink et al. 2000; Stasi and Azar 2007).

Contraindications

Contraindications to LTK are along similar guidelines of poor candidacy for refractive surgery in general. Pregnant or nursing women are prone to fluctuations. Autoimmune or connective tissue disease, such as systemic lupus erythematosus, polyarteritis nodosa, and rheumatoid arthritis, is at higher risk of prolonged inflammation, poor wound healing, and even corneal melt with perforation. The ocular surface in cicatricial disorders, severe dry eye or atopic disease, and chemical burns are also potentially problematic for wound

healing. Other conditions which may be considered relative contraindications for LTK include herpetic keratitis, corneal scarring or dystrophy within the central optical zone, glaucoma, amblyopia, insulin-dependent diabetes, and systemic immunodeficiency (Stasi and Azar 2007).

Techniques and Principles

The concept behind thermokeratoplasty is based within the corneal ultrastructure of collagen fibrils packed into parallel lamellae in a bedding of glycosaminoglycans. By dry weight, collagen comprises 71% of stroma. Therefore, changes in the chemical structure of collagen with heat application will subsequently alter macro-level cornea and topography.

The specific response of corneal collagen to heat depends on the intensity of temperature rise. Low amounts of corneal heating induce transient changes, if any at all. Collagen shrinkage, which is a disruption to the hydrogen bonds of its tertiary structure, occurs within a narrow range of 55–58 °C for humans. Beyond 78 °C, the contraction effect transitions to collagen relaxation as cross-links are hydrolyzed. Further heating beyond this point leads to necrosis and tissue destruction (Stasi and Azar 2007).

Thermokeratoplasty utilizes collagen contraction from heating into the 60 °C therapeutic zone to achieve a refractive effect of corneal flattening. Centrally applied heat causes central flattening, inducing an overall hyperopic shift that may be desirable in conditions such as myopia and keratoconus. Conversely, peripheral heating in either an annular or radial pattern induces central steepening that is applicable for treatment of hyperopia. A third function of thermokeratoplasty is the astigmatic effect of heating at only a specified meridian. For example, steepness at the 90° axis can be countered by applying heat to the periphery of the flatter 180° meridian, thus generating central steepening at the 180° meridian and neutralizing the original astigmatism (Stasi and Azar 2007). In general, the refractive effect is proportional to the number of burns performed.

The contact probe type of Ho:YAG LTK is made by Summit Technology (Waltham, MA). It employs infrared energy (2.06 μm) with pulse power of 19 mJ at 300 μs duration and repetition frequency of 15 Hz. Heat delivered through the probe's tip results in a subsequent cone-shaped zone of corneal shrinkage with approximate parameters of 700 μm diameter at the surface of corneal touch and 450 μm depth of penetration (Stasi and Azar 2007).

Sunrise Technologies (Fremont, CA) produces a noncontact type of Ho:YAG LTK. It operates at 2.13 μm wavelength which pulses at 250 μs duration with frequency of 5 Hz. The laser system is mounted to a slit lamp and able to deliver one to eight treatment spots simultaneously, each about 600 μm in size. To increase refractive effect, a second ring of treatment spots can be placed in addition to the first round. Alternatively, energy intensity and spot size can also be adjusted to alter treatment effect (Stasi and Azar 2007).

On the horizon is low-energy noncontact Ho:YAG LTK with intraoperative wavefront monitoring. This combination of Sunrise Hyperion laser with Shack-Hartmann wavefront sensor (Wavefront Sciences COAS) was first used at Cole Eye Institute in Cleveland, Ohio. Its advantage over conventional LTK is lower-energy application which reduces corneal tissue necrosis, regression, and induced subsequent astigmatism. Thus far, the real-time dynamic wavefront readings do not interfere with laser delivery and appears promising for future relay of wavefront information into intraoperative treatment strategy (Stasi and Azar 2007).

Outcomes

Contact Ho:YAG LTK

Contact type of Ho:YAG LTK can be used for mild to moderate hyperopia. In general, there is a transient phase of overcorrection initially after treatment which is followed by regression of this myopic shift and finally stabilization at 4–6 months postoperatively. Tutton and Cherry's study in 1996 placed two rings of eight laser spots

at 6.5 mm and 9 mm from the central visual axis for up to +4.0 D of hyperopia in 22 eyes. An average of +2.10 D of hyperopic correction was achieved in 17 eyes with no induced astigmatism. However, significant astigmatism (1.25–2.50 D) was produced in 23% of eyes requiring further astigmatic LTK correction. In this series, regression occurred in approximately 50% of cases by 2 years post-LTK, but they reported that many patients read remarkably well in the first few months (Tutton and Cherry 1996). Several other trials also experienced significant regression and lack of treatment predictability.

In regard to hyperopic astigmatism, LTK generates an overall myopic shift in the spherical equivalent of roughly half the amount of the astigmatic correction. In an investigation by Thompson of 26 eyes with astigmatism ranging from 1.5 to 4.0 D, the mean astigmatic correction achieved at 6 months post-op was 1.7 D. This method involved applying four spots, two on each side of the flat meridian at an 8.5 μM ablation zone (Stasi and Azar 2007).

Ho:YAG LTK can also be used as a secondary procedure on eyes with prior ocular surgery such as cataract extraction (CE), photorefractive keratectomy (PRK), laser-assisted in situ keratomileusis (LASIK), and penetrating keratoplasty (PK). Eggink et al. conducted a study that reported efficacy regarding LTK treatment of PRK overcorrection on seven patients with postoperative hyperopia and nine patients with astigmatism. They reported success for both of these conditions, achieving spherical correction of the hyperopia, although two of the seven eyes had induced astigmatism. As for astigmatic correction, the amount of correction was generally reduced with increasing diameter size of the treatment zone, and all eyes with significant improvement demonstrated overcorrection in the first initial postoperative phase. Overall, these authors offered holmium LTK as a useful option for the treatment of astigmatism and overcorrection hyperopia after PRK. However, the results are prone to low predictability and induced astigmatism (Eggink et al. 2000). In 1995, Hennekes reported his experience of astigmatic LTK on eyes with previous CE, PRK, and PK. Results included regression to almost baseline within 1 week and marked overshoot in astigmatic power of about 15 D. The author cautioned against over-interpretation of this small case series, but did express a probable higher propensity for large regression of astigmatic LTK in eyes with large corneal or corneoscleral full-thickness scars (Hennekes 1995).

Noncontact Ho:YAG LTK

Phase IIa and III US trials were conducted on 612 eyes from 379 patients to investigate the treatment of hyperopia with noncontact Ho:YAG LTK. The study aimed to achieve emmetropia in the 3–6 month postoperative period since refractive regression was highest during the first 3 months (0.3 D per month) but essentially leveled off by 6 months thereafter (0.02–0.06 D per month). This goal was accomplished in 62.5% of eyes which were within 1.00 D of emmetropia. The remaining eyes were all undercorrected, and retreatment was performed in ten of these patients. This extended US trial overall concluded that noncontact Ho:YAG LTK is a safe and effective method to correct mild to moderate (+0.75 to +2.50 D) hyperopia with very low risk of complications. An additional advantage of the noncontact system is preservation of untouched cornea allowing future laser in LASIK, PRK, and contact lens use (Stasi and Azar 2007).

Canadian investigators further pursued a phase III clinical trial of noncontact Ho:YAG LTK in 38 eyes with +0.77 D to +2.50 D of hyperopia and up to 1.00 D of astigmatism. At the final 2-year follow-up, 100% of eyes were within 1.0 D of intended refractive state and 92% within 0.5 D. The authors concluded noncontact Ho:YAG LTK as a safe and effective treatment of low hyperopia with predictable refractive results despite a tendency toward regression by 2 years (Rocha et al. 2003).

Astigmatic and myopic correction with noncontact Ho:YAG LTK is still ongoing investigations. Koch et al. described treatment of up to 4.0 D of astigmatism but with only 6 months of follow-up. In the case of myopia, there is an added challenge of central corneal haze and/or

opacification from the treatment which may be vision impairing, unlike that of mid-peripheral hyperopic and astigmatic treatments (Stasi and Azar 2007).

Complications

In general, higher temperatures of thermokeratoplasty not only alter collagen structure but also induce inflammation, corneal vascularization, epithelial thinning, and irregularity as well as stromal scarring (Stasi and Azar 2007). Other potential problems include persistent epithelial defects, infectious keratitis, recurrent erosions, corneal edema, pain, transient elevation in intraocular pressure, and mild foreign body sensation (Stasi and Azar 2007). Overall, Ho:YAG LTK is considered safe with most complications relating to failure to achieve primary goal of the procedure, namely, regression, induced astigmatism, and undercorrection (Hennekes 1995; Tutton and Cherry 1996; Eggink et al. 2000; Rocha et al. 2003; Stasi and Azar 2007).

Cross-References

► Wave Front Analysis

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Holmium-YLF Solid-State Laser

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Definition

Holmium YLiF4 (Ho:YLF) is a solid-state laser with a Ho^{3+} ion doped in yttrium lithium fluoride crystal as the active medium. Holmium-doped solid-state lasers are one of the popular approaches for generating 2 μm laser radiation where Ho:YLF lasers are mainly suited for low pulse repetition frequency (few 10s of Hz) Q-switched application.

Emission Wavelength

The specific emission wavelength for Ho:YLF lasers is 2064 nm.

Pumping Method

Most popular method for pumping these lasers is to use thulium-doped lasers, which in turn are pumped by diode lasers.

Medical Applications

Water has an absorption peak at 2064 nm; hence, Ho-YLF laser is highly absorbed by biological tissue resulting in low penetration depth. When a tissue is irradiated with Ho-YLF laser, due to its low penetration depth, the damage to the surrounding tissue is minimal. Therefore, these lasers are suited for making clean and precise incision and tissue ablation.

Cross-References

► Solid-State Lasers

Holthouse-Batten Chorioretinitis

► Doyne's Honeycomb Dystrophy

Homocystinuria

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Definition

The term "homocystinuria" designates a biochemical abnormality, not a specific disease entity. There are many causes of homocystinuria. All affect one of the transsulfation pathways that convert the sulfur atom of methionine into the sulfur atom of cysteine. This pathway is the chief route of disposal of methionine.

Etiology

The most common defect, cystathionine β-synthase (CBS) deficiency, results in high concentrations of serum methionine (Kaye and The Committee on Genetics 2006a, b). One form of CBS deficiency is responsive to vitamin B6. Other metabolic variants of homocystinuria include defects of Vitamin B12 uptake or activation and tetrahydrofolate reductase deficiency. Two mechanisms probably explain most of the clinical symptoms seen: Firstly abnormal (hyper) coagulation because of "sticky" platelets; and secondly direct toxicity of homocysteine and its metabolites, causing endothelial cell damage.

Clinical Presentation

Clinical problems include multiple, recurrent thromboembolism. Arterial or venous thromboses may involve the cerebral, pulmonary, renal, and myocardial circulation. Patients may also show developmental delays/mental retardation, seizures, psychiatric disturbances, osteoporosis with bone deformities, scoliosis, high palatal arch, muscle weakness with a shuffling gait, and a marfanoid habitus. Ectopia lentis is the outstanding ophthalmic feature of homocystinuria and is detected in approximately 90% of patients. Ectopia lentis has been detected in patients of all age groups. Other reported ophthalmic complications of homocystinuria include retinal detachment, microphthalmos, optic atrophy, peripheral cystoid retinal degeneration, retinal artery occlusion, band keratopathy, and secondary glaucoma.

The potential for early clinical diagnosis is limited. Ocular abnormalities, because of their distinctive lens displacement, may lead to the diagnosis. The diagnosis should be considered in any child or young adult with thromboembolism affecting both the large and small arteries as well as the veins, particularly in association with developmental disabilities, mental retardation, or skeletal findings. Most patients, however, have nonspecific features so that definitive testing involving the measurement of serum or urine amino acids is not accomplished before the expression of more severe clinical symptoms.

Diagnostics

The specific enzymatic defect should be identified. However, all heritable forms of homocysteinuria exhibit autosomal recessive inheritance. Prenatal diagnosis is available for CBS deficiency using cultured chorionic villus cells or amniotic fluid cells to measure the activity of the enzyme. The chromosome map location is 21q22. More than 90 different disease-associated mutations of the CBS gene have been identified. The vast majority of these mutations are "private" mutations that occur in only a single or a very small number of families. The most prevalent mutations are the G307S and I278T mutations. Affected patients vary widely in the extent to which they manifest clinical abnormalities, suggesting considerable genetic heterogeneity. Some of the variability is accounted for by the

relative reduction of enzymatic activity. Absent to relatively low residual activity (up to 10%) of CBS has been noted among different families. However, there are reports of individuals with the identical genotype resulting in a different phenotype within the same family.

Differential Diagnosis

As some of the patients with homocystinuria express a marfanoid habitus, the main differential diagnosis is Marfan syndrome (Summers et al. 2006). Patients affected by Marfan syndrome do not exhibit developmental delays or mental retardation. Seizures or psychiatric diseases are also rare in Marfan syndrome. Measuring blood methionine levels will easily distinct Marfan syndrome from homocystinuria. As ectopia lentis together with glaucoma and cataracts are the main ophthalmological findings, all diseases with ectopic lenses (i.e., Stickler syndrome, Ehlers-Danlos syndrome, Weill–Marchesani syndrome, autosomal dominant ectopia lentis, and autosomal recessive ectopia lentis with or without ectopic pupils) have to be considered in the differential diagnosis.

Prophylaxis

Newborn screening using the bacterial inhibition assay (BIA) test or direct methionine assay may be used to detect increased concentrations of blood methionine. Normal values for serum methionine concentration are noted to be less than 2 mg/dl. Approximately 1 in 5000 infants is found to have blood methionine concentration more than 2 mg/dl. Increased concentrations of methionine may be minimal during the first 3 days of life until there is adequate protein intake (milk feedings). This is especially true in patients who are responsive to vitamin B6, who usually have some residual enzyme activity. It may therefore be preferable to screen for this disorder at 2–4 weeks of age. Early discharge at 24 h or even 18 h results in many missed cases and decreases screening effectiveness.

Recent evidence has shown that carriers (heterozygotes) for homocystinuria have an increased risk of thromboembolic events. Therefore, genetic counseling and screening should be offered to relatives of persons with homocystinuria.

Therapy

Treatment seems to reduce the risk of thromboembolic episodes. Because this is the major cause of mortality and morbidity in these patients, the survival rate may improve with early, effective treatment. Treatment depends on the underlying cause of homocystinuria. As first step, pyridoxine (vitamin B6) responsiveness should be ascertained, because approximately 50% of patients respond to large doses of this vitamin. Nonresponsive patients with CBS deficiency should be treated with methionine-restricted, cystine supplemented diet. Folic acid and betaine therapy may also be helpful with all patients. In the disorders of cobalamin metabolism and transport in which methylmalonic acid and homocystein appear in the urine, hydroxycobalamin treatment (vitamin B12) may be beneficial. Aspirin and dipyridamole have also been used to decrease the occurrence of thromboembolic phenomena. These thromboembolic phenomena are more prone to occur during anesthesia, surgical procedures, and prolonged immobilization.

The management of the main ophthalmic complication (ectopia lentis) is not easy (Harrison et al. 1998). Recurrent lens dislocation in the anterior chamber is the main indication for surgery followed by pupillary block glaucoma. Prophylactic peripheral iridectomy was not successful in preventing lens dislocation into the anterior chamber in 5/45 patients in one larger series. Other ocular complications include optic atrophy, iris atrophy, anterior staphylomas, lenticular, and corneal opacities.

Prognosis

Death has been reported within the first year of life. Approximately 50% of untreated individuals

die by 25 years of age; death is frequently a result of thromboembolic events. Developmental delay is reported in 65–80% of untreated individuals.

The incidence of the mental retardation may be prevented or reduced by treatment. For patients with classic (homozygous) homocystinuria, early treatment with good biochemical control (lifetime plasma-free homocysteine < 11 μmol/l) seems to prevent mental retardation, ectopia lentis seems to be delayed, and the incidence of seizures is reduced. Programs continue to evaluate the efficacy of screening and early treatment. Improvement in screening to decrease the numbers of missed cases is important.

Epidemiology

Although homocystinuria is a rare disorder, carriers of the condition represent a much larger population. If one assumes a worldwide incidence of 1 in 300,000 individuals, the expected carrier frequency is 1 in 135. Because carriers are more prone to thromboembolic events, ascertainment of these individuals via identification of an affected person needs to be emphasized to primary health care professionals.

Cross-References

- ▶ Ectopia Lentis
- ▶ Marfan Syndrome
- ▶ Thrombophlebitis, of Orbital Vein

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Honeycomb-Shaped Corneal Dystrophy

▶ Thiel-Behnke Dystrophy

Hordeolum

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Synonyms

Stye

Definition

Acute infection involving either the meibomian glands (internal hordeolum) or glands of Moll or Zeis (external hordeolum). Infection is typically caused by *Staphylococcus aureus*.

Cross-References

▶ Chalazion

Horizontal Eyelid Shortening

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Synonyms

Lateral canthoplasty; Lateral tarsal strip

Definition

In cases of horizontal laxity of the eyelid, surgically shortening and tightening the eyelid in its horizontal dimension, usually via a lateral tarsal strip procedure.

Indication

Horizontal eyelid shortening and tightening is indicated when horizontal eyelid laxity is present, often in combination with involutional ectropion, involutional entropion, and/or floppy eyelid syndrome. Horizontal laxity can be diagnosed clinically by utilizing the snap and distraction tests.

Contraindication

Any shortening of the eyelid should be conservatively performed. Aggressive resection of tissue can cause problems with secondary rounding and phimosis of the lateral canthal angle.

Techniques and Principles

After the degree of horizontal eyelid laxity is determined with the snap and distraction tests, surgery to horizontally shorten and tighten the eyelid is undertaken. Simple block excision away from the canthus can be performed for horizontal shortening; however, shortening is usually performed as part of the lateral tarsal strip procedure. A canthotomy and cantholysis are performed to allow free mobility of the eyelid. A tarsal strip is then fashioned by denuding the epithelium of the strip along the eyelid margin and posterior lamella; the anterior lamella is then recessed leaving a tarsal strip devoid of epithelial tissue. Conservative shortening of the strip may be performed at this point if desired, particularly in cases of floppy eyelid syndrome. A double-armed suture is then passed in a horizontal mattress fashion through the superior and inferior aspects of the tarsal strip. The upper and lower limbs of the suture are then passed so as to incorporate a purchase of periosteum of the inner aspect of the lateral orbital rim in the region of Whitnall's tubercle. This mattress suture is then tied under surgical tension. The skin incision from the lateral canthotomy is then closed.

Outcome

This maneuver results in horizontal tightening of the eyelid with improved eyelid position.

Complications

Aggressive resection of eyelid tissue at the lateral canthus can cause problems with secondary rounding and phimosis of the lateral canthal angle. Weakening of the orbicularis oculi muscle may occur if there is injury to the zygomatic branch of the facial nerve.

Cross-References

- ▶ Canthal Reconstruction
- ▶ Cantholysis
- ▶ Canthotomy
- ▶ Tenzel Flaps

References

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Horizontal Fracture

- ▶ Guerin (Maxillary) Fracture

Horizontal Fracture (Le Fort I)

► Le Fort Fractures

Horizontal Gaze Center

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Synonyms

Lateral gaze center; Paramedian pontine reticular formation and abducens nucleus

Definition

The horizontal gaze center is a functional unit of neurons that generate coordinated, conjugate horizontal eye movements. Primarily, it includes the paramedian pontine reticular formation (PPRF) and the abducens nucleus in the pons. The PPRF is located on the medial aspect of the pontine reticular formation about 2 mm from the midline. The PPRF receives input through polysynaptic connections from the vestibular nuclei and contralateral frontal lobe for saccades. In addition, the PPRF contains most of the burst neurons that generate horizontal saccades. Neurons from the PPRF project to the ipsilateral abducens nucleus where they synapse with motor neurons of the lateral rectus and internuclear neurons. These interneurons send signals via the medial longitudinal fasciculus (MLF) to the contralateral medial rectus motor neurons resulting in a conjugate lateral gaze. Activation of the right PPRF will result in rightward gaze and activation of the left PPRF results in left horizontal gaze. Lesions in the PPRF may thus impair or limit horizontal conjugate eye movement.

The PPRF also projects saccade-related neurons to the cerebellum and reticulospinal neurons which mediate head movements and eye-head coordination.

Cross-References

► Saccadic Nystagmus

Further Reading

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Horn Cells

► Keratinocytes: Overview

Horner Syndrome

► Anisocoria of the Small Pupil
► Anisocoria of Small Pupil: Horner Syndrome

Horner's Syndrome

► Anisocoria of the Small Pupil

Horner-Trantas Dots

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Definition

Horner-Trantas dots are collections of eosinophils and cellular debris along the limbus of patients with limbal vernal keratoconjunctivitis.

Etiology

Horner-Trantas dots occur in the limbal vernal keratoconjunctivitis subset of vernal conjunctivitis.

Clinical Presentation

Limbal vernal keratoconjunctivitis is more common among black patients. On slit-lamp examination, one would find intraepithelial and subepithelial deposits of eosinophils and cellular debris at the limbus of the cornea.

Diagnosis

Horner-Trantas dots can be diagnosed by finding white intraepithelial and subepithelial deposits at the limbus in patients with limbal vernal keratoconjunctivitis.

Differential Diagnosis

The differential diagnosis for Horner-Trantas dots are staphylococcal hypersensitivity or infectious corneal infiltrates.

Prophylaxis

There is no prophylaxis for Horner-Trantas dots.

Therapy

Horner-Trantas dots are not themselves treated as they do not become visually significant. However, the treatment for vernal keratoconjunctivitis is antihistamine, mast cell stabilizers, or even steroid topical agents.

Prognosis

The prognosis for Horner-Trantas dots is very good as they do not become visually significant. As the limbal vernal keratoconjunctivitis is treated and controlled, the Horner-Trantas dots will subside.

Epidemiology

Vernal conjunctivitis is usually seen in younger patients. Specifically, limbal vernal keratoconjunctivitis is more common among black patients.

Cross-References

► Vernal Conjunctivitis/Keratoconjunctivitis

Further Reading

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Horton's Arteritis

► Arteritic Ischemic Optic Neuropathy

Hospital Addiction Syndrome

► Munchausen Syndrome

HPV

► Human Papilloma Viruses, Ocular Infection

Hruby Lens

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Definition

Additional negative lens for use with slit lamp. The strong negative power of ca. −58.6 D compensates for the eyes' own refractive power, so ocular fundus can be examined binocular with the slit lamp. It can be used as noncontact additional lens.

The instrument was invented by Karl Hruby in 1941.

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HSV

► Herpes Simplex Virus

HSV Endotheliitis

► Disciform Keratitis, Herpes Simplex Virus Causing

HSV Keratitis

► Disciform Keratitis, Herpes Simplex Virus Causing

Hudson-Stähli Line

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Synonyms

Iron line

Definition

Intracellular iron deposition in the corneal epithelial cells which appears as a horizontal line of faint yellow to dark-brown discoloration in the inferior aspect of the cornea (Farjo and Sugar (n.d.)).

Etiology

Iron deposition is a result of pooling of tears in the regions of topographic irregularities, which allows iron from the tear film to be deposited within the epithelium over time (Palay 2011).

Clinical Presentation

Faint yellow to brown horizontal line found close to where the lid margins of the upper and lower lids meet when blinking (Farjo and Sugar (n.d.); Palay 2011). The prevalence increases with age and it is best seen using either cobalt blue or ultraviolet light. For this reason you may first notice it during a slit-lamp examination using fluorescein and cobalt blue illumination (Farjo and Sugar (n.d.); Palay 2011).

Diagnosis

This is a clinical diagnosis. The faint yellow to brown line is found on close examination of the corneal epithelium using the slit lamp with either white light or cobalt blue light.

Differential Diagnosis

1. Vortex keratopathy
2. Iron lines related to previous corneal surgeries
3. Previous corneal trauma
4. Epithelial melanosis related to limbal pigmented cells (e.g., melanoma)

Prognosis

Incidence is higher in the older population, but it is not visually significant.

Epidemiology

The line is seen in 29–90% of persons aged 60 years or more and it can be unilateral in 50% of people.

Cross-References

► Iron, Corneal Deposits of

References

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Hughes Procedure/Modified Hughes Procedure, in Eyelid Repair

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Synonyms

Lid sharing procedure; Tarsoconjunctival graft

Definition

Eyelid sharing procedure for extensive lower eyelid reconstruction, entailing advancement of a tarsoconjunctival flap from the upper eyelid to reconstruct a posterior lamella defect of the lower eyelid.

Indication

Utilized for the reconstruction of extensive (usually greater than 50%) lower eyelid defects, which involve the eyelid margin. Provides vascularized posterior lamellar tissue for full thickness eyelid reconstruction.

Contraindication

An intact healthy upper eyelid is required for the reconstruction. The flap will remain closed for several weeks obstructing vision out of the ipsilateral eye, therefore a seeing contralateral eye is required for vision. The Hughes flap should be avoided in monocular patients or in children at risk of amblyopia development.

Techniques and Principles

Extensive lower eyelid defects require reconstruction for comfort and protection of the eye. On occasion, these extensive lower eyelid defects mandate utilization of an otherwise normal upper eyelid for reconstruction in the form of a Hughes procedure.

Surgery begins with an assessment of the defect size. By grasping the proximal and distal cut ends of the eyelid with forceps and removing any slack, the defect size can be accurately measured. The upper eyelid is everted over a Desmarres retractor and the upper eyelid tarsus inspected. As much upper eyelid tarsus as possible should be left in place to ensure adequate structural support for normal upper eyelid function remains. An incision with a scalpel through

tarsus only, 4 mm below its upper border, will leave a large amount of tarsus in situ in the upper eyelid while providing approximately 4 mm of tarsal tissue to be grafted into the lower eyelid. The dissection is then carefully carried superiorly in a subconjunctival plane avoiding any buttonholes in the conjunctiva, which could compromise vascular supply to the graft. Care should be taken to leave as little Mullers muscle as possible on the tarsoconjunctival flap as this can contribute to upper eyelid retraction after flap separation. The dissection is carried superiorly towards the fornix until the tarsoconjunctival is freely mobile; back-cuts are created medially and laterally to facilitate mobilization. The tarsoconjunctival flap is then advanced into the lower eyelid posterior lamellar defect. The distal and proximal cut ends of the tarsus are sutured to the tarsus of the advancement flap with interrupted longer-lasting absorbable sutures such as vicryl or dexon. Care should be taken to assure the sutures are passed in a lamellar fashion to avoid any potential exposure to and/or abrasion of the cornea. The anterior lamellar is then reconstructed with either a local myocutaneous advancement flap or full thickness skin graft (e.g., upper eyelid, postauricular, preauricular, supraclavicular, etc.) depending on the size of the anterior lamellar defect and status of and laxity of the surrounding tissues.

The tarsoconjunctival flap is left closed to ensure adequate vascularization for several weeks. The tarsoconjunctival flap is then severed 1–2 mm above the anticipated new lower eyelid margin to allow for some degree of contraction. The residual conjunctiva of the flap is then repositied into the superior fornix and trimmed if necessary.

Outcomes

This is a two-stage procedure, which can often achieve a functional lower eyelid capable of providing adequate protection of the globe when extensive tissue loss is present. The reconstructed eyelid is devoid of lashes.

Complications

One of the most common complications of the procedure is upper eyelid retraction, which can on occasion warrant repair. The risk of this complication is theoretically reduced if Mullers muscle is not incorporated in the transposition flap thereby avoiding advancement of the muscle with subsequent retraction. Overly aggressive tarsal resection of the upper eyelid can result in destabilization and subsequent malposition of the upper eyelid. Lower eyelid malpositions such as entropion or ectropion can also occur.

Cross-References

▶ Eyelid Reconstruction

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Human Herpes Virus

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Synonyms

Herpesviridae; HHV; Human herpesvirus

Definition

Herpesviridae are a ubiquitous family of large, enveloped, double-stranded DNA viruses with linear genomes and icosahedral capsids. Human

herpes viruses (HHVs) are particularly notable for their capacity to establish acute, latent, and recurrent infection within a host (Whitley 2012).

Etiology

There are eight known human herpes viruses (HHVs). The HHVs are grouped into three subfamilies given their different viral characteristics, pathogenesis, and disease manifestations. HHV infections are most commonly benign, but HHVs can also cause significant morbidity and mortality, especially in the immunocompromised (Murray et al. 2013).

Human herpes virus-1 (HHV-1) and human herpes virus-2 (HHV-2) are known as herpes simplex virus type 1 and type 2, respectively. These viruses belong to the *Alphaherpesvirinae* subfamily, characterized by their primarily cellular target of mucoepithelial cells and viral spread through direct contact with active, virus-shedding lesions (e.g., cold sores) of mucous and epithelial membranes (Murray et al. 2013). Both HSV-1 and HSV-2 establish latency in neuronal cells, while the former (HSV-1) may also remain latent within cells of the cornea. In regard to ocular disease, HSV-1 and HSV-2 gain access to the trigeminal sensory ganglion during primary infection, where then the virus may enter a latent state and reemerge later on in its lytic phase (Tuli and Kubal 2014).

Human herpes virus (HHV-3), or varicella-zoster virus (VZV), also belongs to the *Alphaherpesvirinae* subfamily. VZV establishes latency in neurons, but targets T cells and mucoepithelial cells. In addition to close contact, VZV is transmissible via respiratory droplets (Murray et al. 2013). VZV, similar to HSV-1 and HSV-2, gains access to the trigeminal ganglion via retrograde migration from the skin during primary infection where the virus subsequently remains latent (Tuli and Kubal 2014).

Human herpes virus-4 (HHV-4) is known as Epstein-Barr virus (EBV). EBV, also called kissing disease, belongs to the *Gammaherpesvirinae* subfamily and is transmissible through saliva. EBV primarily targets B cells and epithelial cells and can establish latency or even immortalized infections within B cells (Murray et al. 2013).

Human herpes virus-8 (HHV-8), commonly known as Kaposi sarcoma-related virus, also belongs to the *Gammaherpesvirinae* subfamily and is the least prevalent of the HHVs. Similar to EBV, HHV-8 establishes latency within B cells. It differs, however, insofar as HHV-8 is transmitted through close, often sexual, contact and primarily targets lymphocytes (Murray et al. 2013).

Cytomegalovirus (CMV), or human herpes virus-5 (HHV-5), belongs to the *Betaherpesvirinae* subfamily, primarily targeting monocytes, granulocytes, lymphocytes, and epithelial cells. Transmitted through a host of mechanisms, including close contact, congenital transmission, tissue transplant, tears, and transfusions, CMV establishes latency in monocytes and myeloid stem cells (Murray et al. 2013).

Along with cytomegalovirus (CMV/HHV-5), human herpes viruses-6 (HHV-6), or herpes lymphotropic virus, and human herpes virus-7 (HHV-7) also belong to the *Betaherpesvirinae* subfamily. HHV-6 and HHV-7 are similar in that they both are known to primarily target lymphocytes and establish latency in T cells, and both are transmitted via saliva (Murray et al. 2013).

Human herpes virus-infected tissues usually correspond with predictable anatomic locations, as the primary cellular targets of each virus are relatively specific. HHV tropism can be highly restricted, given the nature of tissue-specific receptors. HHV replication begins upon cell surface receptor interaction with viral glycoproteins, virus-cell fusion, and release of the nucleocapsid into the cytoplasm (Murray et al. 2013).

Of the human herpes viruses, ocular diseases and complications typically arise from HSV-1, HSV-2, VZV, EBV, and CMV (Pavan-Langston 2008).

Clinical Presentation

Similar to the rest of the body, human herpes virus infections of the eye typically correspond to specific anatomic locations as a result of restrictive

tropism of HHV glycoproteins for tissue-specific receptors (Murray et al. 2013).

Herpes simplex infections (HSV-1 and HSV-2) of the eye usually present as disease of the anterior segment. Ocular HSV infections can present with a diverse and very difficult array of complications rooted in both infectious and immune pathogenic mechanisms and may occur as primary infection of a nonimmune host or recurrent infection in an immune or previously immune host (Pavan-Langston 2008).

Primary HSV disease can occur in neonates, children, and adults. In neonates, HSV ocular infection most typically arises as an acute conjunctivitis with frequently associated ulcerative keratitis. HSV ulcerative keratitis of the neonate may be diffuse with characteristic microdendrites, serpiginous epithelial defects, or less ominously as a punctate keratitis. Other detrimental primary, neonatal ocular HSV complications that occur in an acute or subacute timeframe are necrotizing chorioretinitis, optic neuritis, cataracts, and strabismus resulting from CNS damage or phthisis bulbi (Barnes et al. 2010).

Primary ocular HSV infection in children and adults usually arises 3–9 days after exposure and most commonly presents as an acute periorbital skin infection. Primary ocular HSV infection may also present as a keratoconjunctivitis, conjunctivitis, blepharitis, and, uncommonly, iridocyclitis (Barnes et al. 2010). Although very few infected individuals present with overt disease, those who do may have periorbital dermatitis or blepharitis with severe vesicular lesions and hemorrhagic blisters, pseudomembranous follicular conjunctivitis, geographic ulceration, corneal ulceration, and iritis (Tuli and Kubal 2014). Keratitis will develop in the majority of patients and is initially characterized by punctate staining that converts to multiple diffuse microdendritic epithelial defects or serpiginous ulcers within the first day (Barnes et al. 2010).

Recurrent ocular herpes can occur in the forms of blepharitis, conjunctivitis, geographical or dendritic keratitis, sterile corneal neurotrophic ulcerations, trabeculitis, endotheliitis, iridocyclitis, and stromal keratitis (interstitial keratitis, immune rings, limbal vasculitis, and disciform keratitis) (Barnes et al. 2010).

Acute and recurrent varicella-zoster virus (VZV/HHV-3) infection of the eye, also known as herpes zoster ophthalmicus (HZO), can be a devastating ocular disease with many complications. HZO can impact a vast number of ocular tissues, with complications including but not limited to pseudodendritic keratitis, disciform or neurotrophic keratitis, punctate epithelial keratitis, corneal stroma infiltrates, diffuse iridocyclitis, iris atrophy, scleritis and episcleritis, secondary glaucoma, canalicular scarring, neuro-ophthalmic involvement with nerve palsy or hemiplegia, and postherpetic neuralgia (Barnes et al. 2010).

The most common ocular manifestation of cytomegalovirus (CMV) infection is chorioretinitis, the prevalence and severity of which have declined dramatically since the advent of HAART (highly active antiretroviral therapy) in preventing patient progression from HIV to AIDS (Pavan-Langston 2008). Cytomegalovirus infection of the anterior segment, either alone or in conjunction with CMV retinitis, may manifest as a follicular conjunctivitis, iritis, or as asymptomatic linear and stellate endothelial deposits most frequently found in a reticular pattern within the inferior cornea (Pavan-Langston 2008).

While associated with infectious mononucleosis, Hodgkin's disease, African Burkitt's lymphoma, and nasopharyngeal carcinoma, Epstein-Barr virus (EBV/HHV-4) is also associated with anterior segment and neuro-ophthalmic disease. Manifestations of EBV ocular infection may include: papilledema, optic neuritis, cranial nerve palsies, follicular or hemorrhagic conjunctivitis, nodular or flat scleritis, infectious dendritic epithelial keratitis or stromal keratitis, and extranodal natural killer/T-cell lymphomas of the eye (Pavan-Langston 2008).

Diagnostics

Diagnosing viral infections of the eye is usually done by clinical observation alone. When in need of objective data, four common methods are utilized: (1) examination of skin, corneal, or conjunctival scrapings (of the human herpes viruses, this method is most used for HSV-1 and HSV-2);

(2) immunologic and molecular assays; (3) viral culture; and (4) detection of circulating antibodies. Another strategy, used almost exclusively in herpetic ocular disease, is histopathologic analysis of corneal tissue post keratoplasty. Additionally, polymerase chain reaction (PCR) can successfully detect HSVs and VZV in the tear film and corneas of infected patients (Tuli and Kubal 2014).

Differential Diagnosis

The differential diagnosis of all the human herpes viruses is diverse and extensive and with much overlap. Important associations to consider on a differential include human herpes viruses with similar presentations, other forms of microbial keratitis (other viruses, bacteria, and fungi), and much other inflammatory, autoimmune, or oncologic pathology with similar presentation (Barnes et al. 2010).

Prophylaxis

There are many antiviral prophylactic means to help with frequent recurrences, especially for use in patients with bilateral disease, stromal disease, and to assist in high-risk and stressful periods such as other illness, fever, chemotherapy, and ocular surgeries (Pavan-Langston 2008). Prophylaxis for a particular HHV and given symptomatology is relatively specific and warrants investigation of most current, evidence-based best practices. For example, various combinations of antivirals, such as acyclovir, famciclovir, valacyclovir, and a handful of others, should only be used as prophylaxis with certain HHV pathologies and conditions, often in conjunction with other medications like topical steroids or even specialized, therapeutic contacts. With other HHVs, medications, and interventions like these have no prophylactic value (Tuli and Kubal 2014).

The role and implications of vaccines for ocular HHV diseases, such as in the development of an HSV vaccine, is controversial given the failures of many systemic vaccines to induce local ocular immune responses. Yet, in another instance, evidence of vaccine efficacy is more robust regarding the prevention of varicella-zoster infections and progression to herpes zoster ophthalmicus (Pavan-Langston 2008).

Therapy

A wide range of therapies are systematically used in the treatment of ocular human herpes viruses (HHVs), specifically tailored to the HHV infection and its physical manifestation within a given patient. Common treatments include classes of systemic and ocular antivirals, steroids, antibiotics, sympathomimetic and parasympathomimetic agents, immunomodulators, lubricants, glues, analgesics, therapeutic lenses, and others in addition to surgical interventions like penetrating keratoplasty, tarsorrhaphy, and more (Pavan-Langston 2008). Interventions for a given patient with a particular HHV infection and associated symptomatology should be diagnosed and treatment with specific, current, evidence-based interventions provided.

Prognosis

Patient prognosis is highly dependent upon the infectious etiology and can vary greatly with type of human herpes virus (HHV) infection and location of the infection, among many other factors such as general patient health and immunocompetence.

Epidemiology

Human herpes viruses (HHVs), HHV-8 aside, are a ubiquitous family of virus. In regards to HHVs with significant impacts on eye health, herpes simplex viruses (HSV-1 and HSV-2) are the most common cause of corneal blindness in the resource-rich world, with approximately 500,000 cases diagnosed in the United States annually. Ocular manifestations of the disease are largely

caused by HSV-1. Multiple recurrences, however, are far more common with oral or genital HSV infections than with the ocular form of the disease (Pavan-Langston 2008).

Herpes zoster is recurrent infection with varicella-zoster virus (VZV). Up to 20% of the world's population will have herpes zoster in their lifetime, with up to 50% of those who reach 90 years of age having zoster at some point in life. Herpes zoster has a predilection for females over males, with incidence rates increasing with age and highest among individuals over 80 years of age. Furthermore, herpes zoster incidence is four times greater in Whites when compared to Black and Asian ethnic groups. The incidence of herpes zoster is also greater in patient populations with organ transplants, HIV infection, and cancer (Pavan-Langston 2008).

Asymptomatic cytomegalovirus (CMV) is very common among the immunocompetent, with 50–100% of all individuals having antibody presence indicative of previous CMV infection. CMV is the most common virus to be transmitted in utero, with an incidence of 2.2% of all live births. The incidence of CMV among patients with HIV/AIDS has decreased dramatically since the advent of HAART (highly active antiretroviral therapy), dropping from 7.34 cases per 100 patient years in the pre-HARRT era of 1993–1996 to 0.75 cases per 100 patient years or lower since (Pavan-Langston 2008).

Epstein-Barr virus (EBV) has a very high prevalence, with 90% of individuals positive for EBV antibodies by 30 years of age. Half to 85% of children under the age of 4 living in lower socioeconomic conditions are positive for EBV-specific antibodies, and 26–82% of college students are positive (Pavan-Langston 2008).

Cross-References

- ▶ Acute conjunctivitis
- ▶ Blepharitis
- ▶ Cataract, Causes and Treatment
- ▶ Conjunctivitis
- ▶ Corneal Ulceration
- ▶ Cytomegaloviruses, Retinitis
- ▶ Disciform Keratitis, Herpes Simplex Virus Causing
- ▶ Episcleritis: Overview
- ▶ Follicular Conjunctivitis
- ▶ Hemorrhagic Viral Keratoconjunctivitis
- ▶ Herpes Simplex Virus
- ▶ Herpes Zoster Ophthalmicus
- ▶ Herpesviridae
- ▶ Interstitial Keratitis
- ▶ Intraocular Lymphoma
- ▶ Kaposi Sarcoma
- ▶ Keratitis
- ▶ Keratoconjunctivitis: Overview
- ▶ Neurotrophic Keratopathy
- ▶ Optic Neuritis
- ▶ Progressive Iris Atrophy
- ▶ Postherpetic Neuralgia
- ▶ Thygeson's Superficial Punctate Keratitis
- ▶ Scleritis
- ▶ Secondary Glaucoma in Uveitis
- ▶ Stromal Keratitis (Herpetic)
- ▶ Ulcerative Keratitis
- ▶ Uveitis, Iridocyclitis
- ▶ Varicella Zoster Virus
- ▶ Viral Keratitis with Ulceration

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Human Herpesvirus

► Human Herpes Virus

Human Papilloma Viruses, Ocular Infection

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Synonyms

Conjunctival papilloma; HPV; Human papillomavirus; Infectious papilloma; *Papillomaviridae*; Verrucous lesion; Wart

Definition

A wide and ubiquitous group of DNA viruses with over 100 strains, 9 of which most commonly result in benign ocular papillomatous lesions of the conjunctiva, eyelid margin, and skin of the eyelids

Etiology

Human papilloma viruses (HPVs) are members of the Papillomaviridae family, a group of nonenveloped viruses characterized by double-stranded circular DNA and enclosed in an icosahedral capsid measuring approximately 55 nm in diameter (Douglas 2012). HPVs cause disease through aberrant cell growth. Some strains are considered to be high risk, associated with high-grade squamous intraepithelial lesions and genital tract cancers, and others low risk given their association with warts and other low-grade squamous intraepithelial lesions.

In regard to ocular disease, HPV strains 6 and 11 are most commonly involved in infections of mucous membranes and less frequently HPVs 16, 18, and 33. HPV strains 1–4 most commonly infect skin sites. Papilloma infection with multiple subtypes has also been described (Pavan-Langston 2008).

Infection is spread between individuals through fomites and direct contact with a given site, although conjunctival inoculation through this means of transmission is still under investigation. Further autoinoculation may occur and the resultant spread can lead to multicentric HPV infection. For neonates, direct contact with infected maternal tissues or fluids is a suggested mode of transmission (Douglas 2012).

The role of human papilloma virus in neoplastic transformation of ocular epithelial cells is unclear. While studies have noted that HPVs are found in approximately one third of samples of normal conjunctival tissue, other studies have identified the presence of HPV mRNA at a higher frequency in ocular lesions of patients with conjunctival intraepithelial neoplasia. Other studies have also shown that HPV infection may be associated with a number of other neoplastic and non-neoplastic ocular diseases, including in situ squamous cell carcinoma, invasive squamous cell carcinoma, sporadic retinoblastoma, climatic droplet keratopathy, and scarred corneas (Pavan-Langston 2008).

Clinical Presentation

Human papilloma viruses typically cause benign ocular changes in the form of fleshy, red-pink, sessile (broad-based), or pedunculated (narrow-based) lesions with "fingerlike" projections (Lang 2000). Lesions of the conjunctiva are more commonly reddish in color and those of the skin, grayish. Pedunculated lesions are more often found in children and frequently arise in the fornix and sessile lesions in adults and the bulbar conjunctiva, respectively, but either may occur in any age group and in any part of the conjunctiva. Papillomatous HPV lesions may also arise on the skin of the eyelids and on or within the lacrimal sacs, puncta, ducts, or canaliculi (Palazzi 2008). The limbal or corneal surfaces may become involved, but this is unusual and could be related

to other disease processes including superficial punctate keratitis or pannus formation (Pavan-Langston 2008).

HPV papillomas of the bulbar or palpebral conjunctiva commonly lead to continuous foreign-body sensation. Other symptoms less commonly experienced include irritation, mild to moderate itching, tearing, mucoid discharge, hyperemia, blurred vision, and photophobia. Larger lesions have the propensity to cause punctate epithelial erosions or diffuse keratitis, given the interference with eyelid apposition and tear-film integrity. Occasionally, however, no symptoms are experienced at all (Palazzi 2008).

In immunocompromised patients, HPV ocular infection may be more significant. Infectious papillomas may be larger, multiple, and/or bilateral (Pavan-Langston 2008).

Diagnostics

Diagnosis is commonly made by clinical observation and confirmed with biopsy. Histopathology indicative of HPV infection includes papillomatosis with hyperkeratosis, parakeratosis, and acanthosis. Keratinocytes are commonly large and vacuolated with a notable large halo surrounding the basophilic nuclei. Conjunctival papillomas consist of multiple branching fronds, each with a vascular core, all arising from a single broad (sessile) or narrow (pedunculated) base (Palazzi 2008).

Differential Diagnosis

The differential diagnosis includes both benign and malignant lesions. As such, emphasis is placed on the importance of histopathologic analysis to avoid misdiagnosis of malignant tumors, especially in older patients (Palazzi 2008).

Differential diagnosis:

- Capillary hemangioma
- Pyogenic granuloma
- Squamous cell carcinoma
- Sebaceous cell carcinoma

Prophylaxis

Recurrences of virally induced conjunctival papillomas and cutaneous warts are common. The immunomodulating effects of cimetidine, a histamine2 receptor antagonist commonly used for peptic ulcer disease, have demonstrated significant regression of diffuse HPV-induced papillomatosis. Recommended oral cimetidine dosing is 30 mg/kg/day divided into three doses, taken for 4 months (Palazzi 2008).

The quadrivalent HPV vaccine may also help provide protection against the ocular effects of strains 6, 11, 16, and 18 (Pavan-Langston 2008).

Therapy

Many HPV-induced papillomas spontaneously regress over the course of 1–2 years, and observation is often deemed suitable for asymptomatic individuals or those with only mild symptoms (Pavan-Langston 2008).

Primary therapy consists of surgical excision, cryotherapy, or both. The use of both modalities helps reduce the frequency of further seeding and recurrence, which is common. One surgical strategy to avoid seeding and recurrence includes initial cryotherapy followed by lesion elevation and excision at the papilloma stalk base with inclusion of a small area of normal surrounding tissue and subsequent double freeze-thaw cryotherapy to the excised area. Specifically, papillomas of the lid may be treated with electrodesiccation or heat cautery (Pavan-Langston 2008).

Topical agents, like the antimetabolite mitomycin C (MMC) or the immunotherapeutic interferon alfa-2b (IFN α-2b), may also be considered as adjunctive or alternative therapies for diffuse, large, or recurrent lesions. Complications, however, have been seen with excessive MMC use or when used with open conjunctival wounds, and punctal plugs are recommended to prevent damage to nasopharyngeal tissues. While considered a relatively safe and successful alternative treatment for conjunctival papillomas, IFN α-2b is considered to be a suppressive, not curative, therapy and long-term follow-up is required. Moreover,

superficial keratitis may be a possible side effect of IFN α-2b, but seems otherwise a relatively benign, topical drug (Palazzi 2008).

Prognosis

HPV-associated ocular papillomas are largely benign, but recurrence is frequent, and histopathologic confirmation is recommended, especially in adults, to avoid misdiagnosis of malignancies. Adults with long-standing papillomatous lesions should be treated and monitored, as some papillomas may demonstrate malignant transformation. Lesions in children and young adults are nearly always benign (Palazzi 2008).

Epidemiology

Nongenital HPV prevalence data ranges from 3% to 20%, but greater prevalence is noted among HIV-positive and other immunocompromised populations (Douglas 2012). HPV-associated infectious ocular papillomas are more frequently diagnosed in males. There is no predilection for ethnicity. Studies report the frequency of HPV DNA in conjunctival papillomas as ranging from 50% to 100% (Palazzi 2008).

Cross-References

- ▶ Capillary Hemangioma
- ▶ Climatic Droplet Keratopathy
- ▶ Conjunctival Intraepithelial Neoplasia (CIN)
- ▶ Keratitis
- ▶ Pannus/Micropannus
- ▶ Pyogenic Granuloma
- ▶ Retinoblastoma
- ▶ Sebaceous Cell Carcinoma
- ▶ Squamous Cell Carcinoma of Eyelid

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Human Papillomavirus

▶ Human Papilloma Viruses, Ocular Infection

Hurler-Scheie Syndrome

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Synonyms

MPS I-HS

Definition

Hurler-Scheie syndrome is a lysosomal storage disorder, more specifically a type I mucopolysaccharidosis. It is an inherited disorder, resulting from mutations in the lysosomal enzyme α-1-iduronidase. The deficiency leads to intracellular and extracellular accumulation of the glycosaminoglycans (GAGs) dermatan and heparan sulfate, resulting in cell death, tissue damage, and excessive secretion of these GAGs in urine. Hurler-Scheie syndrome is an intermediate form of the disease between the severe Hurler's syndrome and the milder Scheie syndrome. They are thought to have inherited one Hurler and one Scheie gene from each parent (Srinivasan et al. 2011). Both Hurler and Scheie syndromes are autosomal recessive (Arrfa 1997).

Hurler syndrome manifests at 6–12 years of age. They develop gargoyle-like coarse facial features, hypertelorism, skeletal deformities, short stature, large head circumference, communicating hydrocephalus, mental retardation, cardiac complications, and hepatosplenomegaly (Srinivasan et al. 2011). Corneal clouding is a prominent feature of the disease, and its features develop within the first few days to months of birth. Initially the cornea may be clear, but soon afterward it develops an avascular noninflammatory clouding (Arrfa 1997). The opacities are initially fine gray punctate opacities found in the anterior stroma, which progress to involve the posterior stroma and endothelium, forming a diffuse ground-glass haze (Waheed and Azar 2005). The thickness of the cornea may increase secondary to the glycosaminoglycans (Arrfa 1997). Other ocular complications include retinal pigmentary degeneration, glaucoma, optic nerve swelling, and optic atrophy. Corneal transplantation success may be limited by the retinal manifestations of the disease. Most Hurler syndrome patients die within the first decade of life (Srinivasan et al. 2011).

Scheie syndrome is a rare disorder characterized by joint stiffness and deformity of the hands, carpal tunnel syndrome, and aortic valve disease. It is caused by a different defect in the same enzyme affected in Hurler's syndrome, α-1-iduronidase. Ocular signs include progressive severe corneal clouding that is more marked at the periphery but may affect the entire cornea (Arrfa 1997). Proteoglycan material deposits in the stromal lamella, which is characteristic of all mucopolysaccharidoses. The histologic appearance of the cornea in Scheie syndrome is characterized by epithelial breaks with peg-like undulations, marked attenuation of Bowman's layer, and fibrous long-spacing collagen (Srinivasan et al. 2011). They may also develop pigmentary retinopathy, optic atrophy, and glaucoma (Arrfa 1997). Symptoms of Scheie syndrome present between 5 and 15 years of age. These patients have normal height and intelligence (Srinivasan et al. 2011).

Patients with Hurler-Scheie syndrome have an intermediate phenotype between Hurler and Scheie syndrome. They typically have normal intelligence and mild facial changes. Ocular manifestations of the disease include corneal opacification due to accumulation of dermatan and heparan sulfate and retinopathy. They tend to die in their twenties or later secondary to cardiopulmonary disease (Srinivasan et al. 2011).

Cross-References

▶ Primary Congenital Glaucoma

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Hurricane (Vortex) Keratopathy

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Synonyms

Blizzard keratopathy; Vortex keratopathy

Definition

Whorl or vortex pattern given to pattern of corneal surface growth in states of increased replicative epithelial turnover.

Etiology

Turnover of corneal epithelium from stem cells located at limbus.

Clinical Presentation

Most often seen at the epithelium of corneal grafts. Also seen after long-term topical steroid use or deposition of substances like pigment, iron, drug metabolites, and glycogen. In addition seen in patients with no corneal graft but evidence of chronic epithelia breakdown and healing. Whorl pattern is sustained as long as the stimulus for increased cell turnover is maintained. Once the stimulus is eliminated, the pattern tends to resolve spontaneously.

Diagnostics

Highlighted with fluorescein staining of cornea under slit-lamp biomicroscopy

Differential Diagnosis

Differential diagnosis includes corneal verticillata and crystalline keratopathy.

Prophylaxis

Removal of epithelial cell turnover stimulus.

Prognosis

Good.

Epidemiology

Not enough studies.

References

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Hurricane Keratopathy

▶ Cornea Verticillata

Hutchinson-Tay Choroiditis

▶ Doyne's Honeycomb Dystrophy

Hyaline Corneal Degeneration

▶ Keratinoid (Spheroidal) Degeneration
▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
▶ Spheroidal Degeneration

Hyaloid

▶ Vitreous Humor

Hyaluronic Acid, for Dry Eye

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Synonyms

Ophthalmic Viscosurgical Device (OVD)

Definition

Glycosaminoglycan disaccharide composed of repeated units of D-glucuronic acid and *N*-acetyl-

D-glucosamine. It is found in many human tissues including synovial fluid, skin, cartilage, and the vitreous.

Etiology

Studies suggest that hyaluronic acid promotes migration of corneal epithelial cells, but not necessarily proliferation (Gomes et al. 2004).

Clinical Presentation

It can be helpful for cases of moderate to severe ocular surface disease.

Prophylaxis

Hyaluronic acid can be used to lubricate the cornea during ophthalmic surgery.

Therapy

Hyaluronic acid (HA) is a viscoelastic agent often used to lubricate the cornea for ophthalmic surgeries. For patients with moderate to severe dry eyes, 0.4% hyaluronic acid eye drops have been effective in improving the signs and symptoms of dry eyes (Kinoshita et al. 2013). Results have been more dramatic with a hypotonic solution of 0.4% HA(150 mOsm/L) than an isotonic solution (300 mOsm/L) (Koh et al. 2013).

Prognosis

When used as a chronic outpatient treatment for keratoconjunctivitis sicca, 0.4% HA was found to improve tear-break-up time, fluorescein and Rose Bengal staining, Schirmer I scores, tear osmolarity, impression cytology, and patient symptoms. Hyaluronic acid may cause higher-order aberrations due to light scatter for the first 5 min after instillation (Lester et al. 2000).

Cross-References

- ▶ Epithelial Defects
- ▶ Exposure Keratitis/Keratopathy
- ▶ Exposure Staining, Keratoconjunctivitis Sicca
- ▶ Keratoconjunctivitis Sicca
- ▶ Pemphigoid, Cicatricial
- ▶ Punctate Epithelial Defects/Erosions
- ▶ Stevens Johnson Syndrome

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Hydatid Cyst

▶ *Echinococcus granulosus* (Echinococcosis), Orbital

Hydrodissection

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Synonyms

Cortical cleaving hydrodissection

Definition

Hydrodissection and hydrolineation describe lens surgery techniques. This step in cataract surgery succeeds the corneal incision and capsulorrhexis stages.

Hydrodissection causes the dissection of the lens from the cortex which is performed to enable the following emulsification of the lens.

Epidemiology

Hydrodissection has become an integral part of microincisional lens surgery. Because cataract surgery is among the most often performed operation, the frequency of hydrodissection technique is very high today.

History

In 1984, Faust performed first the hydrodissection by placing a cannula beneath a "beer-can" capsulotomy opening.

In 1990, Sheperd reintroduced this technique after the development of the continuous curvilinear capsulorrhexis. He described the method of irrigating fluid into the nuclear-cortical plane and thus allowing nuclear rotation and crosshatch sculpting.

After that, Anis developed the part of hydrodelineation which describes the injection of irrigation fluid into the nucleus to isolate the inner nucleus from epinucleus.

In conclusion, Fine eventually established the hydrodissection technique and named it "cortical cleaving hydrodissection."

Clinical Features

Hydrodissection and hydrodelineation are performed with the same cannula.

Tests

Preoperative requirements compromise an ophthalmological examination of both eyes to determine the nature or severity of cataract. Also visual acuity, refraction, and workup of the patient's anamnesis should be practiced to eliminate possible exclusion criteria for cataract surgery with the phacoemulsification technique.

Differential Diagnosis

Apart from hydrodissection, one can apply the hydrodelineation technique to separate the epinucleus from the endonucleus. Another related method is the viscodissection, used in cases of hard nuclei.

Etiology

See "History" section above.

Treatment

The hydrodissection should be performed through the main incision. BSS fluid is injected under the anterior capsular rim advanced toward the equator using a 25- or 27-gauge blunt cannula attached to a 2 ml syringe. The successful hydrodissection induces a wave of dissection toward the equator and subsequently a wave in the opposite direction under the posterior capsule. Injection should be made in different independent points to prevent, for example, a capsular block syndrome.

Afterward the nucleus should be freely rotating in the capsular bag.

Cross-References

- ▶ Aspiration Curette
- ▶ Capsular Block Syndrome
- ▶ Capsulorrhexis
- ▶ Cataract, Causes and Treatment
- ▶ Cataract Surgery

- ▶ Continuous Curvilinear Capsulorhexis (CCC)
- ▶ Phacoemulsification and Posterior Chamber Intraocular Lens (IOL) Implantation

Further Reading

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Hydrophilic

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Definition

Hydrophilic means having a strong affinity for water, absorbing or dissolving in water (Kohnen et al. 2009).

Epidemiology

See entry "▶ Hydrophilic Acrylic Intraocular Lens."

History

See entry "▶ Hydrophilic Acrylic Intraocular Lens."

Clinical Features

See entry "▶ Hydrophilic Acrylic Intraocular Lens."

Tests

See entry "▶ Hydrophilic Acrylic Intraocular Lens."

Differential Diagnosis

The opposite of hydrophilic is hydrophobic.

Etiology

The term hydrophilic refers to Greek "hydor" = water and "philein" = to love (Kohnen and Koch 2009).

Treatment

See entry "▶ Hydrophilic Acrylic Intraocular Lens."

Cross-References

- ▶ Acrylic Intraocular Lens
- ▶ Cataract Surgery
- ▶ Foldable Intraocular Lens
- ▶ Hydrophilic Acrylic Intraocular Lens
- ▶ Hydrophobic Acrylic Intraocular Lens
- ▶ Refractive Surgery
- ▶ Silicone Intraocular Lens

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Hydrophilic Acrylic Intraocular Lens

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Synonyms

Hydrophilic acrylic IOL; Hydrophilic polyacrylic IOL

Definition

Artificial lens made of transparent hydrophilic acrylic that is implanted in the eye and performs in focusing images. Hydrophilic means that this type of IOL has a strong affinity for water.

Epidemiology

Most of the worldwide-implanted IOLs are made of acrylic today. The most common acrylic IOL however is made of hydrophobic acrylate.

History

See also entries "► Intraocular Lens" and "► Acrylic Intraocular Lens." The first hydrophilic acrylic IOL was implanted in 1983 in Perth, Australia.

Clinical Features

Hydrophilic acrylic IOLs are manufactured from polyhydroxyethyl methacrylate (pHEMA) and have a refractive index of 1.47. Their water content is between 18% and 36%. These lenses are smaller in the dry state and swell on hydration (Barrett et al. 1986; Werner 2008). Advantages of this type of IOL are that they are less harmful to the corneal endothelium, they fold and unfold faster, IOL material is highly compressible due to its water content, mechanical properties are not temperature dependent, IOLs provide very good optical clarity, and they are not expensive. In patients after trauma with underlying uveitis, hydrophilic acrylic IOLs display better biocompatibility than hydrophobic acrylic IOLs. Disadvantages are their high flexibility and reduced tensile strength and high rates of decentration as they lack adhesive property to the lens capsule. Also, the rate of posterior capsule opacification is higher than in hydrophobic acrylic IOLs (Auffahrt 2008).

Tests

During the decades, hydrophilic acrylic IOLs have undergone extensive research and testing in Europe, Asia, and the USA and have been proven safe for the treatment of cataracts and refractive errors.

Differential Diagnosis

Foldable IOLs may also be made of hydrophobic acrylic or silicone.

Etiology

The term hydrophilic refers to Greek "hydor" = water and "philein" = to love. The term acrylic refers to the Latin word "acer" or the Greek word "ákros" that mean "sharp" due to the smell of acrylic acid.

Treatment

See also entries "► Cataract Surgery" and "► Refractive Surgery" describing different IOL implantation techniques.

Cross-References

► Cataract Surgery
► Foldable Intraocular Lens

- ▶ Hydrophilic
- ▶ Hydrophobic
- ▶ Hydrophobic Acrylic Intraocular Lens
- ▶ Intraocular Lens
- ▶ Silicone Intraocular Lens

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Hydrophilic Acrylic IOL

- ▶ Hydrophilic Acrylic Intraocular Lens

Hydrophilic Polyacrylic IOL

- ▶ Hydrophilic Acrylic Intraocular Lens

Hydrophobic

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Definition

Hydrophobic means resisting to combine with water or unable to dissolve in water (Kohnen et al. 2009).

Epidemiology

See entry "▶ Hydrophobic Acrylic Intraocular Lens".

History

See entry "▶ Hydrophobic Acrylic Intraocular Lens".

Clinical Features

See entry "▶ Hydrophobic Acrylic Intraocular Lens".

Tests

See entry "▶ Hydrophobic Acrylic Intraocular Lens".

Differential Diagnosis

The opposite of hydrophobic is hydrophilic.

Etiology

The term hydrophobic refers to greek "hydor" = water and "phobos" = fear (Kohnen and Koch 2009).

Treatment

See entry "▶ Hydrophobic Acrylic Intraocular Lens".

Cross-References

- ▶ Acrylic Intraocular Lens
- ▶ Cataract Surgery
- ▶ Foldable Intraocular Lens
- ▶ Hydrophilic Acrylic Intraocular Lens

- ▶ Hydrophobic Acrylic Intraocular Lens
- ▶ Refractive Surgery
- ▶ Silicone Intraocular Lens

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Hydrophobic Acrylic Intraocular Lens

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Synonyms

Hydrophobic acrylic IOL; Hydrophobic polyacrylic IOL

Definition

Artificial lens made of transparent hydrophobic acrylic that is implanted in the eye and performs in focusing images. Hydrophobic means that this type of IOL is resisting to combine with water or unable to dissolve in water.

Epidemiology

Most of worldwide implanted IOLs are made of acrylic today. The most common acrylic IOL is made of hydrophobic acrylate.

History

See also entries "▶ Intraocular Lens" and "▶ Acrylic Intraocular Lens." The first acrylic IOL was implanted in 1983.

Clinical Features

Hydrophobic acrylic IOLs are made of copolymer of phenylethyl acrylate and phenylethyl methacrylate. They have a refractive index of 1.55 and their water content is below 1%. Advantages of hydrophobic acrylic are the reduced rate of posterior capsule opacification and the higher refractive index that results in thinner lens thickness. Disadvantages are their tacky nature to surgical instruments, their susceptibility to mechanical damage, and their reduced optical clarity compared to hydrophilic acrylic IOLs (Kohnen and Koch 2009; Auffahrt 2008; Werner 2008).

Tests

During the decades, hydrophobic acrylic IOLs have undergone extensive research and testing in Europe, Asia, and the USA and have been proven safe for the treatment of cataracts and refractive errors.

Differential Diagnosis

Foldable IOLs may also be made of hydrophilic acrylic or silicone.

Etiology

The term hydrophobic refers to Greek "hydor" = water and "phobos" = fear. The term acrylic refers to the Latin word "acer" or the Greek

word "ákros" that mean "sharp" due to the smell of acrylic acid.

Treatment

See also entries "▶ Cataract Surgery" and "▶ Refractive Surgery" describing different IOL implantation techniques.

Cross-References

- ▶ Cataract Surgery
- ▶ Foldable Intraocular Lens
- ▶ Hydrophilic
- ▶ Hydrophilic Acrylic Intraocular Lens
- ▶ Hydrophobic
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Hydrophobic Acrylic IOL

▶ Hydrophobic Acrylic Intraocular Lens

Hydrophobic Polyacrylic IOL

▶ Hydrophobic Acrylic Intraocular Lens

Hydrops, Keratoconus

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Synonyms

Acute hydrops keratoconus; Corneal edema

Definition

Acute hydrops is caused by a rupture in Descemet's membrane that allows an influx of aqueous into the cornea.

Etiology

Hydrops is often seen or discussed in the context of keratoconus. Keratoconus is a progressive ectasia, or thinning, of the corneal stromal tissue. As the cornea thins, it becomes structurally weaker and progressively will come forward with increasing astigmatism. This bulging forward can be demonstrated by Munson's sign, Rizzuti sign, or serial topography or keratometry. This progression puts stress and strain on Descemet's membrane and endothelium. In patients with advanced keratoconus, breaks in Descemet's membrane may occur, providing channels for the aqueous humor to pass into the stroma, resulting in marked corneal edema. This is known as acute hydrops and presents clinically as a sudden onset of pain and loss of vision.

Descemet's membrane is the basement membrane of the corneal endothelium. Descemet's membrane is composed mainly of type IV and VIII collagen and does not regenerate after injury. It is synthesized by endothelial cells and assembled at the basal surface. Ultrasound biomicroscopy of keratoconic eyes with acute

hydrops reveals intrastromal clefts connected to the anterior chamber, which separate the stroma from the ruptured Descemet's membrane. These clefts may develop simultaneously or immediately after the rupture of Descemet's membrane (Abbey and Yoo 2010). There is also separation between the stroma and Descemet's membrane caused by these clefts. This extra level of separation represents a focal area of Descemet's detachment. This could lead to delayed closure and slower resolution of stromal edema.

If acute hydrops occurs, patients will present with a sudden onset of blurry vision and intense foreign body sensation with photophobia. As the corneal swells, there can be secondary epithelial breakdown and risk for secondary corneal infection. Slit-lamp biomicroscopy demonstrates diffuse opacification of the corneal stroma and injection of the conjunctiva. The corneal stroma may appear protuberant and very thickened. There may also be epithelial breakdown over the area of stromal edema.

The opacification often resolves without intervention over the course of 6–10 weeks, but scarring commonly occurs after the edema resolves. In the acute phase, patients may have some relief from hypertonic drops or ointment as well as cycloplegic agents. As the edema improves, comfort and clarity of the cornea improve. However, residual scarring occurs along with changes to astigmatism. Non-resolution of the opacification, poor best corrected visual acuity, unstable contact lens, and contact lens intolerance are all indications for penetrating keratoplasty. A history of acute hydrops can be a contraindication to performing a deep anterior lamellar keratoplasty (DALK) for keratoconus.

Histopathology of post-keratoplasty corneal buttons 4 months after the onset of hydrops demonstrated significant stromal edema. The rupture and detachment of Descemet's membrane resulted in the formation of ledges or ridges (Stone et al. 1976). As the detached areas heal, new endothelium migrates and covers the exposed areas of stroma. The areas of ledges are covered as well. During this time, the endothelium regenerates basement membrane.

Hydrops is often seen or discussed in the context of keratoconus. However, other causes of spontaneous breaks of Descemet's membrane include obstetric forceps injury, congenital glaucoma, Terrien marginal degeneration, and pellucid marginal degeneration. Allergy and eye rubbing are risk factors for the development of hydrops.

Patients with congenital glaucoma are often referred to the ophthalmologist because of corneal edema. Because infants have immature and growing collagen that makes up the cornea and sclera, increased intraocular pressure can result in profound ocular enlargement. As the corneal diameter increases, collagen fibers in Descemet's membrane are exposed to the increased tension. As the cornea stretches, Descemet's membrane and the overlying corneal endothelium may tear. This results in aqueous access to corneal stroma and cornea edema or acute hydrops. With time, edema resolves and endothelial cells migrate over the breaks and lay down new basement membrane. Following this, ridges develop along the separated edges of Descemet's membrane and can be seen clinically. This line of double striae is called Haab's striae.

Children with congenital glaucoma often present due to the cornea edema that causes the triad of epiphora, blepharospasm, and photophobia. Other presenting findings of children with congenital glaucoma include progressive unilateral myopia.

Occurrence

It occurs in approximately 3% of keratoconic eyes (Tuft and Buckley 1994).

Classification

Hydrops is an acute event with variable amount of corneal swelling and symptoms of discomfort. Although the break usually heals within 6–10 weeks and the corneal edema clears, a variable amount of stromal scarring may develop. Hydrops is not typically classified, but can be followed with serial examinations, with corneal thickness maps (anterior segment ocular coherence tomography, ultrasound pachymetry,

Pentacam), or by following corneal curvature with topography.

Cross-References

- ▶ Keratoconus
- ▶ Primary Congenital Glaucoma

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Hyperacuity (Vernier Acuity)

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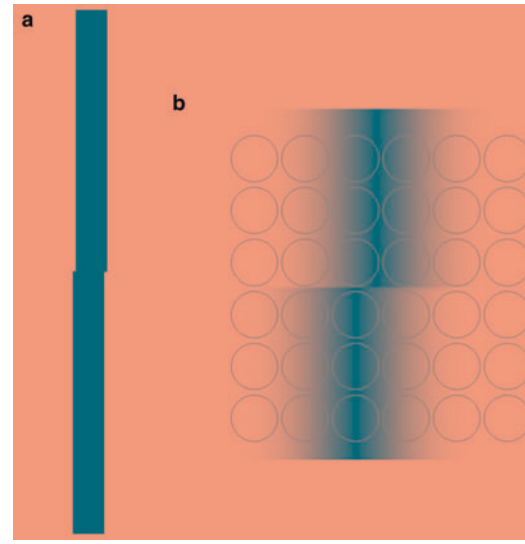
Synonyms

Nonius acuity; Vernier acuity

Definition

Under optimum conditions, spatial offsets of 2″ to 6″ can be recognized in high-contrast targets. Because the angle of the offset is finer than expected from the spacing of foveal photoreceptors, this type of visual acuity is called hyperacuity. One example of hyperacuity is Vernier acuity, which is determined by recognizing a just notable break in two lines vertically aligned (Fig. 1a). One explanation for the much higher resolution is the detection of contrasts above and below the break (Fig. 1b). There are other forms of hyperacuity such as spatial interval acuity and the detection of a single point relative to a circle.



Hyperacuity (Vernier Acuity), Fig. 1 Vernier acuity. (**a**) Setup with two vertically aligned bars with horizontal offset. (**b**) Different stimulation of cones in the region above and below the break allows detection of the break even in case of a vertical offset below the cone spacing

Hypercalcemia: Corneal Changes

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Synonyms

Calcific band keratopathy; Hypercalcemia-induced band keratopathy; Metabolic band keratopathy

Definition

Hypercalcemic states can induce a form of corneal degeneration characterized by a horizontal band of intracellular calcium deposits, typically at Bowman's layer, confined to the interpalpebral fissure (Chang et al. 2011).

Etiology

Calcific band keratopathy is a common corneal degenerative condition that can present at any age. While often the secondary result of chronic corneal diseases like uveitis and juvenile rheumatoid arthritis, band keratopathy may also occur secondarily to elevated serum calcium or phosphate (Woodard et al. 2014). Hypercalcemic states that lead to corneal changes may originally be induced by a number of systemic conditions, including but not limited to sarcoidosis, metastatic neoplasms to bone, vitamin D toxicity, hyperparathyroidism, and secondary hyperparathyroidism to chronic renal failure (Woodard et al. 2014).

The exact mechanism of calcium salt precipitation and deposition within the cornea is unclear. Theories include the following: (1) aberrations of normal corneal metabolism lead to increased tissue pH and calcium precipitation; (2) evaporation of tears results in calcium salt deposition within the interpalpebral zone; and (3) carbon dioxide release leads to pH increase and subsequent calcium deposition (Woodard et al. 2014). In the case of hypercalcemia-induced band keratopathy, calcium is deposited as hydroxyapatite salt intracellularly and can be found upon histopathologic examination both intranuclearly and intracytoplasmically. Fine basophilic granules typically present first at the level of Bowman's layer. The granules eventually coalesce and then fragment Bowman's layer, in time replacing the superficial corneal stroma. Throughout the subepithelial tissue, hyaline-like material is deposited among the calcium precipitate, which gives the appearance of Bowman's layer duplication. Moreover, a fibrous pannus may also develop as a result of the calcification that further disrupts the Bowman's layer-epithelium interface, leading to atrophy of the epithelium (Chang et al. 2011).

In cases of chronic ocular inflammation, the lesion may begin centrally. With band keratopathy resulting from hypercalcemia, however, the peripheral form of the disease is observed in which the lesion periphery is well demarcated and separated from the limbus by a lucent zone. The lucent zone is thought to be the result of either the buffering capacity of limbal vessels preventing calcium salt precipitation or that the limbal region simply lacks Bowman's layer. As the multifocal deposits coalesce, clear circles void of calcium salts can be seen where penetrating corneal nerves traverse Bowman's layer (Chang et al. 2011).

Calcium lesions in hypercalcemia-induced band keratopathy progress slowly over months to years. Patients diagnosed with dry eye, however, can progress much more rapidly on the order of weeks given increased tear calcium concentration and that dry eye may encourage calcium deposition near the corneal surface (Chang et al. 2011).

Clinical Presentation

Visible on ophthalmologic exam, patients frequently present with calcium deposits in the form of a horizontal band that typically originates near the corneal periphery at the 3 and 9 o'clock positions and progresses centrally (Chang et al. 2011). While patients in the early stages of calcific band keratopathy secondary to hypercalcemia may be asymptomatic, later stages result in decreased vision, pain, persistent foreign body sensation, photophobia, tearing, or recurrent corneal erosions (Chang et al. 2011).

Diagnostics

Diagnosis is commonly made by clinical observation. Typically, the associated disease causing calcific band keratopathy is already known. In patients for whom the etiology is unknown, ocular and systemic causes should be sought through

history taking, ocular examination, and laboratory studies. A thorough history, including questions regarding vitamin, calcium, and alternative supplement intake, should be elicited. Physicians may consider obtaining serum calcium, phosphorus, uric acid, and renal function measurements, as well as labs for parathyroid hormone (PTH) and angiotensin-converting enzyme (ACE), when trying to establish a potential systemic cause of calcific band keratopathy (Chang et al. 2011).

Differential Diagnosis

The differential diagnosis for general and disease-associated causes of band keratopathy is extensive and includes (Chang et al. 2011):

Chemicals, eye drops, and irritants
Chronic nongranulomatous uveitis (juvenile rheumatoid arthritis)
Congenital hereditary endothelial dystrophy
Discoid lupus erythematosus
Dry eye syndromes
Fanconi's disease
Hypercalcemic states
Hyperparathyroid states
Hyperphosphatasia
Hypophosphatasia
Ichthyosis
Idiopathic causes
Inherited disease
Interstitial keratitis
Intraocular silicone oil
Lithium
Mercury vapors
Metastatic disease (lung and bone disease with increased calcium)
Milk-alkali syndrome (Albright-Burnett)
Multiple myeloma
Nephropathic cystinosis
Norrie's disease
Other chronic ocular diseases
Other systemic diseases
Paget's disease
Phthisis bulbi (degenerated globe)
Prolonged corneal edema
Prolonged glaucoma
Proteus syndrome
Sarcoidosis
Spheroid degeneration
Still's disease
Thiazides
Trachoma
Tuberous sclerosis
Tumoral calcinosis
Uremia
Viscoelastics
Vitamin D toxicity

Prophylaxis

Prophylaxis for hypercalcemia-induced calcific band keratopathy includes monitoring systemic and ocular health for prevention of hypercalcemic states that lead to calcium salt deposition in the cornea (Chang et al. 2011).

Therapy

Treatment is indicated if the patient is symptomatic, for example, experiencing limited vision or discomfort. The mainstay of treatment is initial administration of topical anesthetic and subsequent superficial keratectomy with or without calcium deposit chelation via application of 0.4% ethylenediaminetetraacetic acid (EDTA) to the deepithelialized cornea. Superficial keratectomy entails a careful stripping of the calcific scale with forceps, dry cellulose sponges, and diamond burr or number 15 blade until the cornea becomes clear (Kenyon et al. 2014).

Other treatment modalities include the use of excimer laser keratectomy and lamellar keratoplasty or application of amniotic membranes (Kanski et al. 2008). Excimer laser has successfully been used to improve vision through clearing the visual axis. While scalpels are required to remove calcifications of rough band keratopathy, laser has been used directly on some smooth band keratopathies with success. Amniotic membranes may be used in order to quickly establish a stable ocular surface following surgical removal of the calcific band keratopathy (Chang et al. 2011).

Prognosis

Reepithelialization of the cornea may take many days. Recurrence after therapy is not uncommon, especially in those with systemic conditions. In patients with calcific band keratopathy secondary to hypercalcemia, reports exist of incomplete regression upon serum calcium level normalization (Chang et al. 2011).

Epidemiology

The exact prevalence or incidence of calcific band keratopathy secondary to hypercalcemia is not reported.

Cross-References

- ▶ Angiofibromas, Facial, in Tuberous Sclerosis
- ▶ Band Keratopathy
- ▶ Congenital Hereditary Endothelial Dystrophy
- ▶ Corneal Edema
- ▶ Dry Eye Syndrome
- ▶ Disodium Ethylenediaminetetraacetic Acid
- ▶ Hypercalcemia-Induced Band Keratopathy
- ▶ Interstitial Keratitis
- ▶ Light Toxicity
- ▶ Sarcoidosis
- ▶ Secondary Glaucoma in Uveitis/Inflammatory Eye Disease
- ▶ Silicone Oil
- ▶ Spheroid Degeneration
- ▶ Trachoma
- ▶ Viscoelastic Agents

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Hypercalcemia-Induced Band Keratopathy

▶ Hypercalcemia: Corneal Changes

Hyperemia, Conjunctival

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Synonyms

Conjunctival injection

Definition

Conjunctival hyperemia is a conjunctival reaction that appears as dilation and redness of the conjunctival vessels. The pattern of hyperemia often appears with the greatest redness at the fornices and fades moving toward the limbus.

Etiology

The hyperemia occurs in the conjunctiva. The conjunctiva is divided into bulbar, palpebral, and forniceal conjunctiva. Histologically, this is divided into the epithelium and substantia propria (stroma). The epithelium is a non-keratizing epithelium with goblet cells (Kanski and Bowling 2011). The substantia propria is vascularized with a superficial adenoid layer containing lymphoid tissue and a deeper fibrous layer with connective tissue (Kanski and Bowling 2011;

Lindquist 2011). The conjunctival hyperemia occurs in this vascular substantia propria, and these conjunctival vessels arise from the palpebral and anterior ciliary arteries (Kanski and Bowling 2011; Lindquist 2011). Since the conjunctiva is transparent and the underlying sclera is white, these dilated vessels can easily be seen.

Conjunctival hyperemia can occur actively or passively. Active hyperemia, also called arterial hyperemia, occurs when the blood flow through the conjunctival vessels increases due to vasodilation. Normally, vessels are in a slightly constricted, vascular tone. The vasodilation that deviates from this resting vascular tone may occur because of membrane potentials or action by the autonomic nervous system and norepinephrine (Efron 2012). In contrast, passive hyperemia, also called venous hyperemia, is due to obstruction of flow. The obstructed vessel dilates proximally, becoming a red, dilated vessel.

Occurrence

Conjunctival hyperemia is present in numerous conditions, which makes it a very common symptom. Environmental factors like smoke, wind, allergies, and chemical fumes can cause hyperemia (Kanski and Bowling 2011; Lindquist 2011). Additionally, infections with many types of viruses and bacteria will also cause conjunctival hyperemia. Conjunctival hyperemia is also common in contact lens wearers and is thought to be due to metabolic influences, chemical influences, or allergies to the contacts or the solutions used (Efron 2012).

Classification

The classification of conjunctival hyperemia helps distinguish this symptom from more serious conditions that involve tissue deeper to the conjunctiva. Since the conjunctiva is only firmly attached to the tarsal plate and not firmly attached on the bulbar surface, the conjunctiva and its vasculature are freely mobile over the bulbar surface. That is in contrast to the vessels underling the conjunctiva, which are not mobile. Another test of diagnostic utility is that these conjunctival vessels will blanch with topical phenylephrine (Lindquist 2011). These two characteristics can be important in distinguishing conjunctival hyperemia from other vascular symptoms seen in pathology like scleritis.

Once it is determined that the conjunctival vessels are involved, conjunctival hyperemia often is characterized by numerical grading and location. The physician may also designate the location of hyperemia by the region of the affected conjunctiva (bulbar, forniceal, or palpebral) and by using a clockface description. It is often the presence of other signs and symptoms like pain, papillae, follicles, or discharge that leads to the diagnosis.

Cross-References

- ▶ Allergic Conjunctivitis
- ▶ Conjunctivitis

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Hyperkeratosis

- ▶ Cutaneous Horn+B2658

Hypermetropia

- ▶ Hyperopia

Hyperopia

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Synonyms

Farsightedness; Hypermetropia; Longsightedness

Definition

Hyperopia is a disproportion between the axial length of the eye and its refractive power, whereas the individual refractive power is too small in respect to the individual eye's axial length (Fig. 1) (Moore et al. 2008).

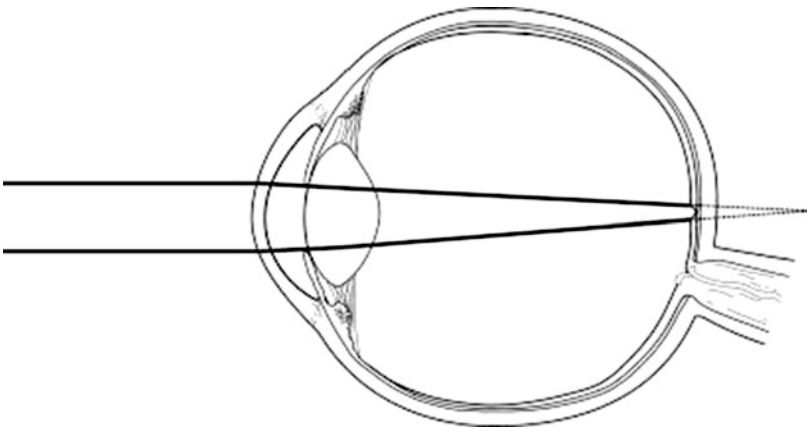
Basic Characteristics

Theoretically hyperopia, and accordingly myopia, can be classified as axial or refractive hyperopia. Whereas axial hyperopia represents a too short axial length of the eye in relation to a "normal" refractive power of the eye, refractive hyperopia represents a "normal" axial length associated with too much refractive power. The phrase "normal" in this context refers to an eye model (i.e., the *Gullstrand's* normal eye). As such eye models are derived from empirical data, the individual's eye usually differs from the "normal" assumptions. Hyperopia thus is usually a combination of both, axial and refractive errors, with axial errors representing the major component.

Table 1 summarizes the different classification schemes of hyperopia, according to the American Optometric Association guidelines (Moore et al. 2008). Looking at this table, it becomes clear that the major difficulty in diagnosing hyperopia is the accommodative ability of young patients' eyes which can only be overcome by cycloplegia.

Incidence

Due to the variations in classifying hyperopia as shown in Table 1, different studies provide different prevalence of hyperopia. Age, however, has a major influence on the prevalence of hyperopia. While infants show a Gaussian distribution of hyperopia, with 4–9% at 6–9 months of age having hyperopia of +3.25D or more (Moore et al. 2008; Atkinson et al. 2007), in the one-year-old population, the value decreases to 3.6% (Moore et al. 2008; Ingram et al. 1986). Higher levels of astigmatism in childhood are also associated with hyperopia, seeming to decrease from the age of five. From then on, the prevalence of hyperopia declines (5–20 years), with increasing prevalences of myopia. Latent hyperopia often



Hyperopia, Fig. 1 Schematic cross-sectional illustration of a hyperopic eye. The refractive power of the eye is too low to focus parallel light rays on the retina. Instead, there is a virtual focus behind the eye

Hyperopia, Table 1 Classification scheme of hyperopia according to (1)

General clinical classification		
Simple hyperopia	*Due to normal biological variation*	*Axial or refractive etiology*
Pathological hyperopia	*Due to abnormal ocular anatomy*	*Maldevelopment, ocular disease, trauma*
Functional hyperopia	*Paralysis of accommodation*	
Classification in accordance to refractive error		
Low hyperopia	*≤ +2.00 D*	
Moderate hyperopia	*+2.25 D to +5.00 D*	
High hyperopia	*> +5.00 D*	
Classification in accordance to the role of accommodation		
Facultative hyperopia	*Can be overcome by accommodation*	
Absolute hyperopia	*Cannot be compensated by accommodation*	
Classification in accordance to the effect of cycloplegia		
Manifest hyperopia	*Determined by noncycloplegic refraction*	*Facultative or absolute*
Latent hyperopia	*Detected only by cycloplegia*	*Facultative*
Simple functional classification		
Significant hyperopia	*Causes symptoms*	
Insignificant hyperopia	*Causes no symptoms*	

becomes significant with the onset of presbyopia. Prevalence differs significantly among certain ethnicities, native Americans, African Africans, and Pacific islanders being among the groups reported to have the highest prevalences, East Asians the lowest (Moore et al. 2008; Post 1962).

Causes

Causes for hyperopia are a combination of hereditary factors and biologic variation (Moore et al. 2008; Hammond et al. 2001). Physiological hyperopia hardly ever develops after childhood. Pathologic hyperopia is associated with diabetes mellitus, contact lens wear, and a host of intraocular and orbital tumors and inflammations; it can thus be acquired at any age (Moore et al. 2008).

Therapy

In case of insignificant hyperopia, no treatment is required, because. In case of significant hyperopia, classical treatment includes first glasses and contact lenses. Surgical options include laser in situ keratomileusis (LASIK) and to a somewhat lesser extent photorefractive keratectomy (PRK), phakic intraocular lens (PIOL) implantation, and refractive lens exchange (RLE) (Kohnen et al. 2008).

Cross-References

- ▶ Ametropia: Definition
- ▶ Astigmatism
- ▶ Choroidal Neovascularization: Myopia
- ▶ PIOL
- ▶ Presbyopia
- ▶ PRK
- ▶ Refractive Lens Extraction (RLE)

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Hyperopic Shift

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Synonyms

Farsighted shift

Definition

Hyperopic shift after keratorefractive surgery, especially after radial keratotomy.

Epidemiology

In the Prospective Evaluation of Radial Keratotomy (PERK) study, 43% of 693 eyes underwent a hyperopic shift of one diopter or more 10 years postoperatively (Waring et al. 1994).

History

With the introduction of refractive procedures to ophthalmic surgery, mostly after radial keratotomy was established in the late 1970s (Akpek et al. 2002).

Clinical Features

Shift towards farsighted vision.

Tests

Visual acuity, refraction, corneal topography.

Differential Diagnosis

Physiologic age-related hyperopic shift, hyperopic shift resulting from corneal distortion or trauma, contact lens wear, chemical or thermal burn, Adie's pupil, cycloplegic agents, ectopia lentis, cataract, and retinal or orbital pathologies.

Etiology

Progressive hyperopic shift due to weakening of the paracentral cornea, resulting in iatrogenic keratectasia.

Treatment

Spectacle or contact lens correction (Glazer and Azara 2002).

Cross-References

- Adie's Pupil (Tonic Pupil), Pharmacologic Testing
- Ectopia Lentis
- Keratectasia
- Laser In Situ Keratomileusis
- Radial Keratotomy
- Refractive Surgery
- Topography (Corneal)

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Hyperornithinemia with Gyrate Atrophy (HOGA)

► Choroid, Gyrate Atrophy of

Hyperplastic Persistent Pupillary Membrane. (Some authors consider these to be different than persistent pupillary membranes. See Clinical Relevance below.)

► Persistent Pupillary Membrane

Hypoalphalipoproteinemia

► Tangier Disease, Corneal Changes

Hyposphagma

► Subconjunctival Hemorrhage

Hypotony

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Synonyms

Ocular hypotony

Definition

Intraocular pressure lower than episcleral venous pressure.

Differential Diagnosis

Hypotony may be caused by decreased production of aqueous due to inflammation, medications, or proliferative vitreoretinopathy. Hypotony may also result from aqueous loss either external, such as following surgery or trauma, or internal, as in cyclodialysis cleft or retinal detachment. Treatment of hypotony is most effective if the underlying cause can be addressed.

Cross-References

► Retinal Detachment

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Hysterical Amblyopia

► Nonorganic Visual Loss

Iatrogenic Ectasia

► Ectasia, Corneal

Ice Pack Test for Myasthenia Gravis

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Definition

The ice pack test can sometimes be used to help determine if ptosis (drooping eyelid) is possibly due to myasthenia gravis (MG). MG is an autoimmune neuromuscular disease in which antibodies block, bind, or modulate acetylcholine receptors at the neuromuscular junction. Ocular MG (OMG) leads to variable, fluctuating ptosis and extraocular muscle weakness and fatigue. Ptosis is a common presenting symptom of MG, and the ice pack test can be done easily and safely in the clinic. It is unclear why decreased temperature improves function of the levator palpebrae muscle in myasthenic ptosis but several hypotheses have been proposed.

The Test

An ice pack is placed on the ptotic eyelid for several minutes and if positive may result in transient improvement of ptosis that is secondary to MG. Another common presentation of MG is diplopia due to extraocular muscle weakness and ophthalmoplegia may also improve with ice testing on the eyelid, but the test is less effective for diplopia in MG. The ice test has moderate sensitivity but relatively high specificity for MG-related ptosis.

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Ice Pick Headaches

► Ice Pick Pains

Ice Pick Pains

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Synonyms

Ice pick headaches; Ophthalmodynia periodica

Definition

Ice pick pains are a form of primary headache that is characterized by brief and intense episodes of idiopathic stabbing pains (jabs and jolts) that may recur throughout the day. It may be felt primarily or radiate to the eye. The episodes are typically brief lasting between 5 and 30 s. While less prevalent than other primary headaches such as migraines, they may be disabling.

Clinical Presentation

The pain of ice pick headache (IPH) is typically localized and unifocal and often occurs at the temple or orbit. IPH is not usually associated with underlying disease or systemic condition. Interestingly, IPH can occur in up to 40% of individuals with migraines. Symptoms of IPH are usually limited to intermittent, transient, stabbing pains in well-defined areas.

Therapy

Treatment for IPH usually starts with nonsteroidal anti-inflammatory drugs (NSAIDs), but other analgesic therapyies may be required in severe cases.

Further Reading

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ICE Syndrome

► Iridocorneo Endothelial Syndrome

ICK

► Crystalline Keratopathy, Infectious

ICL

► Collamer Intraocular Lens

Idiopathic Central Serous Retinopathy/Chorioretinopathy

► Central Serous Chorioretinopathy/Choroidopathy

Idiopathic Facial Palsy

► Bell's Palsy

Idiopathic Facial Paralysis

► Bell's Palsy

Idiopathic Furrow Degeneration

► Furrow Degeneration, Senile

Idiopathic Intracranial Hypertension

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Synonyms

Benign intracranial hypertension; Pseudotumor cerebri

Definition

Idiopathic intracranial hypertension (IIH), also commonly known as pseudotumor cerebri (PTC), is a neuro-ophthalmological disorder characterized by increased intracranial pressure (ICP) of undetermined cause. IIH is a diagnosis of exclusion defined by the following in the modified Dandy criteria: (1) signs and symptoms only due to increased ICP (e.g., headache, pulsatile tinnitus, diplopia, transient visual obscurations); (2) an absence of ventricular enlargement or intracranial space-occupying lesions on neuroimaging studies (e.g., secondary to an intracranial disorder, a

meningeal process, or cerebral venous sinus thrombosis [CVST]); and (3) an elevated opening pressure with normal cerebrospinal fluid (CSF) composition on lumbar puncture. We consider patients who develop increased ICP secondary to medication side-effects or cerebral venous sinus stenosis to have a form of secondary PTC and not idiopathic (i.e., IIH) per se (Brazis and Lee 1998).

Etiology

While the exact pathogenesis of IIH remains unknown, various hypotheses have been proposed, including abnormal vitamin A metabolism, dysregulation of adipose tissue mediated cytokine pathways (e.g., leptin), and more recently distal stenosis of the cerebral transverse venous sinus. Obesity and female gender are known associations with IIH but the precise mechanism of elevated ICP in these patients remains ill defined.

Epidemiologically, IIH is a disorder that primarily affects obese women of childbearing age (15–44 years) with an annual incidence of 4–21 per 100,000 independent of geographic location and ethnicity. Risk factors associated with IIH include recent weight gain, exogenous medication usage (specifically corticosteroids, growth hormone, tetracycline derivatives (e.g., minocycline), vitamin A derivatives, and lithium), and a variety of systemic conditions (e.g., iron deficiency anemia, renal failure, Addison's disease, polycystic ovarian syndrome, and systemic lupus erythematosus).

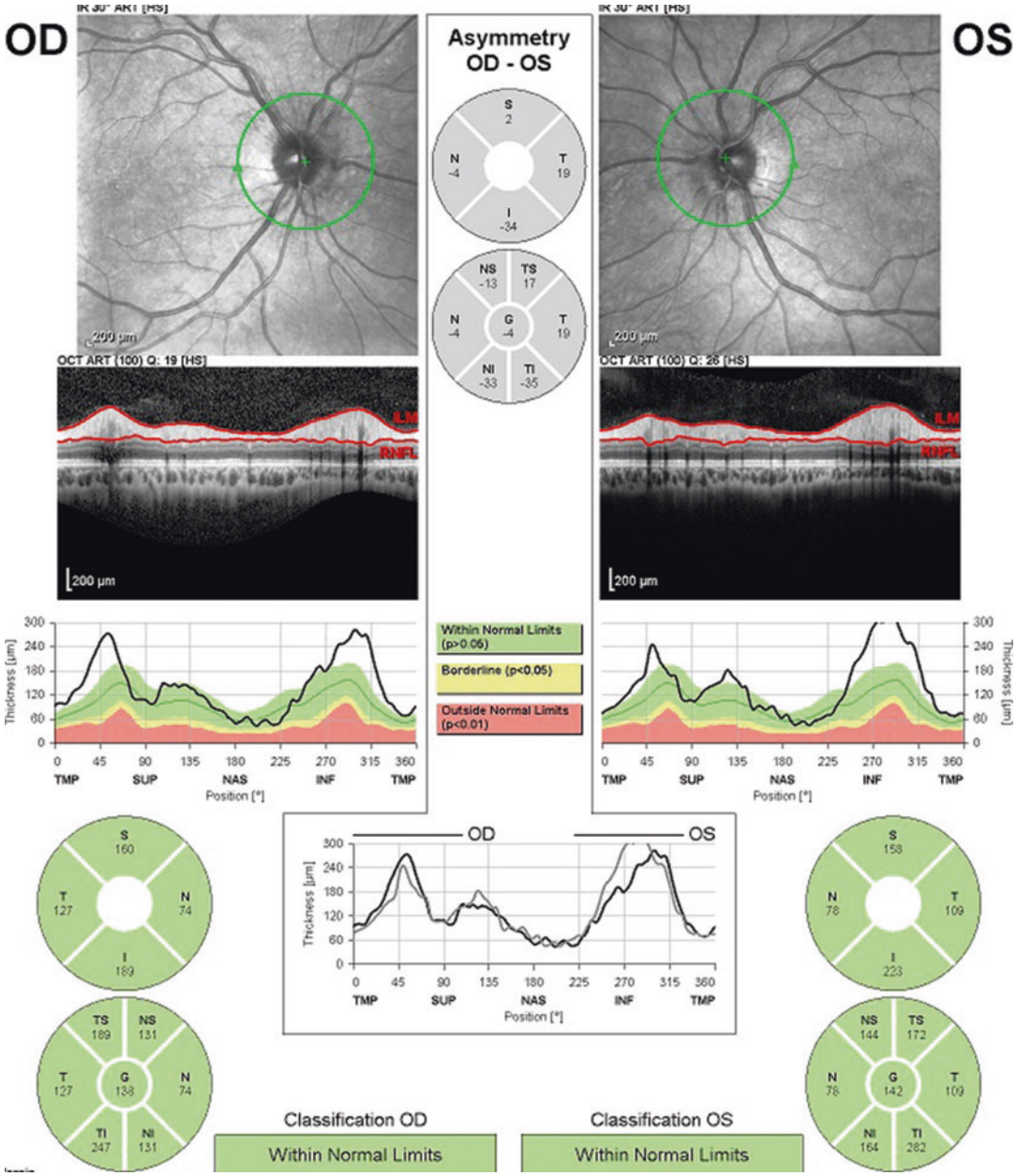
Clinical Presentation

The most common presenting symptom of IIH is a nonspecific headache that may vary in character, location, frequency, and severity. There is no characteristic or defining feature of the headache, however, in IIH. The pain may be facial or retrobulbar in location and may clinically resemble tension, migraine, or rebound headache. In addition, many patients with IIH have concomitant headaches that meet International Headache Society (IHS) criteria for these headache syndromes (e.g., migraine). Other common presenting symptoms of IIH include transient visual obscurations (TVOs) that last for few seconds and may be postural, pulsatile tinnitus, intermittent or constant binocular horizontal diplopia (often due to a sixth nerve palsy as a nonlocalizing sign of increased ICP), and blurred vision.

The most common clinical sign in IIH is bilateral papilledema but papilledema is not required for the diagnosis. Papilledema is often graded using the Frisen scale (from Grade 0 to Grade 5), with higher grades of papilledema and a longer duration of disc edema associated with a higher risk of permanent visual loss. Papilledema, however, may be asymmetric or even absent in IIH. In one study, it was found that up to 10% of patients with IIH had asymmetric papilledema (Spitze et al. 2013). Visual field deficits in IIH most commonly present as enlarged blind spots but any nerve fiber layer type defect can be observed in one or both eyes. Central scotomas (resulting from papillomacular bundle involvement) are rare in patients with IIH and thus patients with a central scotoma should have a careful evaluation of the macula to exclude concomitant macular hemorrhage, edema, subretinal fluid or exudates, or superimposed ischemic optic neuropathy. Patients with unexplained decreased central visual acuity or significant visual field loss from IIH should be considered for more aggressive medical and surgical management including urgent optic nerve sheath fenestration or cerebrospinal fluid (CSF) shunting procedure. Although a nonlocalizing sixth nerve palsy and secondary incomitant esotropia can occur in IIH, any other ocular motility deviation or other cranial neuropathy would be atypical for IIH and should prompt further evaluation for alternative etiologies. In addition, IIH is a noninflammatory condition and the presence of anterior or posterior uveitis should raise the suspicion for an inflammatory mimic of IIH for the findings (e.g., sarcoidosis) (Fig. 1).

Diagnostics

The clinical evaluation of patients with IIH should include a complete history with particular



Idiopathic Intracranial Hypertension, Fig. 1 Optical coherence tomography (OCT) shows mild grade 1–2 papilledema with increased nerve fiber layer on global thickness assessment of 128 microns OD and 142 microns OS. Although the OCT classifies the results as in the "green zone" and "within normal limits" the values in microns are above normal. The black line in the thickness plots represents the patients values and are above the normal thickness for controls

attention paid to secondary causes of increased ICP including medications, hypercoagulable states, infectious processes, and systemic inflammatory processes. An ophthalmic examination should be supplemented with a formal visual field test, dilated funduscopic examination, and (if possible) baseline and follow-up optic nerve photographs. A lumbar puncture (with opening

pressure, cell count and differential, glucose, and protein) is recommended after negative neuroimaging (preferably cranial contrast MRI with MRV) is performed. In patients with papilledema, checking the systemic blood pressure is important to exclude hypertensive optic neuropathy that might mimic papilledema and IIH. Some authors have also recommended a complete blood count (CBC) testing, as severe anemia (typically iron deficiency) may be associated with IIH but this is not yet a universally accepted recommendation. While elevated opening pressure is required for the diagnosis of IIH, some patients have an artificially normal or even low intracranial pressure measurement at the time of lumbar puncture due to faulty technique or perhaps diurnal fluctuation in ICP (e.g., after multiple attempts or fluoroscopic LP performed shortly after failed conventional LP).

Magnetic resonance imaging (MRI) of the brain with and without gadolinium with post-contrast magnetic resonance venography (MRV) is the imaging study of choice for IIH. Several findings on MRI are highly suggestive but not diagnostic of IIH: (1) flattening of the posterior sclera (approximately 80% of patients); (2) empty sella (approximately 70% of patients); (3) distension of the perioptic subarachnoid space by CSF (approximately 50% of patients); and (4) enhancement of the prelaminar optic nerve with gadolinium contrast (approximately 45% of patients). Cerebral venous sinus thrombosis (CVST) should be ruled out prior to the diagnosis of IIH and while MRI may sometimes detect CVST, both computed tomography venogram (CTV) and magnetic resonance venography (MRV) are significantly more sensitive for CVST. We highly recommended an MRV in addition to the cranial MRI even in patients that present as typical IIH. Some patients, however, cannot have an MRI (e.g., extreme obesity, metallic foreign body, pacemaker) or may have contraindication to gadolinium (e.g., renal failure), and in these cases a standard computed tomographic (CT) scan may be the only option.

Differential Diagnosis

Any entity that results in increased ICP may result in a clinical presentation similar to that of IIH. Important secondary causes of increased ICP include:

1. Mass lesions (e.g., tumors, abscesses, hemorrhage)
2. Increased CSF production (e.g., choroid plexus papilloma)
3. Decreased CSF absorption (e.g., subarachnoid hemorrhage, bacterial/fungal meningitis), obstructive hydrocephalus, and cerebral venous sinus outflow obstruction (e.g., cerebral venous sinus thrombosis, jugular vein compression or thrombosis)

In addition, there are conditions that might mimic papilledema (i.e., optic disc edema not due to increased ICP) including malignant hypertension (i.e., hypertensive emergency or urgency), infectious, inflammatory, infiltrative, hereditary, toxic, metabolic, or ischemic optic disc edema, or cases of pseudopapilledema.

Prophylaxis

Non-applicable

Therapy

The mainstay of therapy for IIH is weight loss and medical therapy with acetazolamide (Diamox) typically initially 500 mg QD or BID with increasing dose to maximum tolerance up to 2–4 g as needed. Diamox is our recommended first line agent in treatment of symptomatic IIH (Brazis and Lee 1998; Galgano and Deshaies 2013). Various case series have shown that acetazolamide is effective in symptomatic management and vision stabilization in up to 70% of patients. Although "sulfa allergy" and pregnancy should prompt clinical caution, there is limited evidence to support

not using acetazolamide in patients with non-anaphylactic allergic or adverse reactions to "sulfa" containing agents. Likewise, pregnant patients (especially in the third trimester) might still benefit from medical treatment but consultation with the treating obstetrician should be performed prior to treatment of IIH patients who are pregnant. In general, however, the evaluation and management of pregnant and nonpregnant patients with IIH is the same. Gadolinium contrast for MRI and acetazolamide are FDA class C agents and a risk benefit decision needs to be made on an individual basis for their use in pregnant patients with IIH. In patients on acetazolamide, although serum electrolytes could be routinely followed, most clinicians simply warn the patient and the primary physician about the potential side effects including the risk of metabolic acidosis and kidney stones without routine testing. Furosemide (20–40 mg per day for adults) is often considered a second-line therapy for IIH but has been used effectively in combination with acetazolamide (Brazis and Lee 1998). Thiazide diuretics have yet to show any proven benefit in patients with IIH but might be considered. Topiramate, an antiepileptic medication with carbonic anhydrase inhibition similar in mechanism to that of acetazolamide, is often used as an alternative therapy in patients who cannot tolerate Diamox (Lee and Wall 2012). Clinicians should also be aware that topiramate may cause ocular side effects including angle closure glaucoma and induced myopia. Long-term medical therapy should always be conducted in conjunction with dietary and behavioral modifications (weight loss, exercise, etc.).

The primary indications for surgical intervention in patients with IIH are progressive visual field defects or an intractable headache despite maximum medical therapy (Biousse et al. 2012; Galgano and Deshaies 2013). In addition, some patients may be noncompliant or intolerant to medical treatment. The two main surgical interventions in patients with PTC are cerebrospinal fluid (CSF) shunting procedures (such as ventriculoperitoneal or lumboperitoneal shunt) and optic nerve sheath fenestration (ONSF) (Biousse et al. 2012). Although serial lumbar punctures (LP) may be useful in rare circumstances (e.g., pregnancy, urgent patients prior to surgery, cryptococcal meningitis related papilledema) to temporarily control ICP prior to surgery, we generally advise against serial LP as a sustained or repeated treatment for IIH. The CSF reforms very quickly after an LP and thus there is little theoretic reason for this treatment to work on a long term basis. In addition, serial lumbar punctures are uncomfortable and can result in patient dissatisfaction and various complications, including low-pressure headache, CSF leak, and CSF infection. A lumbar drain, however, might be a reasonable alternative temporizing measure for acute, fulminant IIH with visual loss prior to admission and consideration for definitive surgical treatment of papilledema. Cerebral venous stenting is a relatively new and still controversial procedure based on observations that many typical IIH patients have distal stenosis of the transverse venous sinus. The precise role, indications, and long-term prognosis of stenting in IIH remains to be defined by a controlled clinical trial. The first line surgical intervention for visual loss despite maximum medical therapy in our practice is optic nerve sheath fenestration (ONSF) but CSF shunting may be necessary at institutions where ONSF is not available or perhaps for patients who wish to undergo only a single surgery or who have concomitant intractable headache as the indication for surgery.

Temporary diplopia is the most common complications of ONSF and may be the result of edema or less commonly direct trauma to the extraocular muscles, nerves, or blood supply (Biousse et al. 2012). Transient diplopia occurs in up to 29–35% of ONSF. Other common complications of ONSF include pupillary dysfunction (11%) and temporary decreased visual acuity (11%). Permanent and severe visual loss (e.g., CRAO or optic nerve damage) fortunately are rare after ONSF. Both CSF shunting procedures and ONSF have various other surgical and anesthesia related potential complications, though

ONSF is in general considered a safer and less invasive procedure. ONSF is also the preferred surgical modality in children. Eyes that undergo ONSF often have a recurrence of the initial symptoms (~2 to 32%) and may require repeat surgery.

Although CSF shunting procedures have a higher success rate, the incidence of complications is significantly higher than that of ONSF. Shunt failure occurs in 50–80% of patients, often requiring multiple revisions. Other common complications include shunt infection, abdominal pain, and other postoperative complications. Tonsillar herniation, sunset eyes, and slit ventricle syndrome are rare complications of CSF shunts and, in at least one series, the inpatient mortality for CSF shunting the mortality rate was as high as 0.9% for ventriculoperitoneal shunt and 0.3% for lumboperitoneal shunting.

Prognosis

To date, there is no prospective case series describing the natural history and progression of IIH. In our clinical practice, a clinical course lasting a few months to 1 or 2 years is most common with symptoms gradually regressing with therapy. With treatment, there is often gradual improvement/stabilization within this time interval though most patients are left with persistent residual papilledema and/or residual visual field defects/permanent visual loss. Symptoms recur in as high as 40% of all patients even after years of stability. A small subset of patients present with insidious onset and rapidly progressive IIH (with central visual loss within weeks of symptom onset) classified as fulminant IIH. The visual prognosis is significantly worse for patients with fulminant IIH and aggressive surgical management should be considered at onset in these patients.

Cross-References

- ▶ Benign Intracranial Hypertension
- ▶ Cerebral Venous Sinus Thrombosis (CVST)
- ▶ Pseudotumor Cerebri

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Idiopathic Optic Neuritis

▶ Optic Neuritis: Overview

Idiopathic Polypoidal Choroidal Vasculopathy (PCV)

▶ Polypoidal Choroidal Vasculopathy

IFIS

▶ Intraoperative Floppy-Iris Syndrome

IFS

▶ Interface Fluid Syndrome

Illuminance: Definition

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Definition

Illuminance E_v (unit Lux [lx]) is the total luminous flux or amount of light received by a surface. It is used to specify light levels of room illumination for ophthalmological examination procedures such as contrast sensitivity tests or measuring pupil sizes at standardized light levels. Illuminance takes account for the spectral sensitivity of the human photoreceptors and can be derived from irradiance E_e by $E_v = 683 \frac{lm}{W} \cdot \Sigma V(\lambda) \cdot E_e(\lambda)$ if the spectral distribution of the light is known.

Cross-References

▶ Photoreceptor Cells

Image Quality, General

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Synonyms

Optical quality; Retinal image quality

Definition

The fidelity at which an optical system creates an image of an object. Although the term "optical quality" is used synonymously from time to time, the latter may also include aspects of subjective perception.

Basic Characteristics

Most optical systems are designed to obtain an image that represents the object imaged by the system as exactly as possible. The exactness of imaging and therefore the image quality are affected by the optical phenomena ▶ aberrations, scatter, and diffraction. For measurement, image quality is quantified with reference to the object imaged. Therefore, many image quality metrics are ratios between the characteristics of the actual image and the object. Typical characteristics quantified by metrics are the compactness of the point spread function, the loss of contrast through the optical system, and the unevenness of the ▶ wave front created by the optical system. The image quality of eyes is often referred to as "retinal image quality."

Cross-References

▶ Optical Aberrations

Impending Perforation

▶ Descemetocele

Implantable Collamer Lens

▶ Collamer Intraocular Lens

Implantable Contact Lens

▶ Collamer Intraocular Lens

Implants, Orbital

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Synonyms

Pneumo-orbitism

Definition

Presence of air in the orbit and/or periorbital tissues following orbital wall fracture.

Etiology

Orbital blowout fractures occur when an impact raises intraorbital pressure to the point where the thin bones of the orbital floor and medial wall are "blown out," pushing orbital contents into the maxillary or ethmoid sinus. Orbital emphysema most commonly results (63% of cases) from an orbital blowout fracture (Key et al. 2008). The resulting communication with the paranasal sinuses allows air to accumulate in the orbital space. Sudden onset of orbital emphysema after Valsalva actions (laughing, sneezing, nose blowing) is occasionally reported and is believed to result from the formation of a one-way valve across the fracture site, permitting air to enter the orbit, but not to leave it.

Clinical Presentation

Classically, patients who have had recent trauma to the orbit, face, or head present with sudden onset of one or more of the following after nose blowing, laughing, or other Valsalva actions: periorbital swelling, pain, lid distension, diplopia, and blurred vision. On examination, patients may demonstrate ophthalmoplegia, decreased visual acuity, a tense, hard globe, and proptosis. Intraocular pressure (IOP) is usually elevated. If high intraorbital air pressure results in decreased perfusion to the retina or optic nerve, an afferent pupillary defect may be present (Muhammad and Simpson 1996).

Orbital emphysema may also present as an incidental finding on radiographic assessment; it is detected in up to 50% of orbital fractures on CT scan (Key et al. 2008).

Diagnostics

The diagnosis of orbital emphysema can usually be made from history and physical examination alone. However, distinguishing orbital emphysema from retrobulbar hemorrhage can be difficult; therefore, the diagnosis should be supported by orbital CT scan. IOP should be measured by tonometry, and an assessment of extraocular muscle function should be made.

Differential Diagnosis

Differential diagnosis includes ▶ retrobulbar hemorrhage, ▶ orbital cellulitis, ▶ preseptal cellulitis, ▶ thyroid orbitopathy, ▶ lymphoma, ▶ cavernous hemangioma, and ▶ Wegener granulomatosis (Nerad et al. 2001).

Prophylaxis

Patients with recent orbital and facial trauma, with or without radiographic evidence of orbital wall fracture, should be advised to avoid nose blowing, heavy lifting, laughing, and other Valsalva activities.

Therapy

Orbital emphysema without visual loss is a benign, self-limited condition, which usually resolves in about 2 weeks. Mildly elevated IOP

with no associated visual deficits can be observed or treated medically with IOP-reducing topical agents. However, compressive orbital emphysema with rapidly decreasing visual acuity is an emergency and must be treated promptly to avoid ischemic damage to the retina and optic nerve. Surgical decompression is achieved via lateral canthotomy and cantholysis, which expands the orbital volume and lowers intraorbital pressure. In rare cases, intraorbital needle aspiration may be necessary to relieve compression (Key et al. 2008).

Antibiotics may reduce the incidence of orbital cellulitis in cases of orbital emphysema; however, the benefit of antibiotics remains unproven (Key et al. 2008).

Prognosis

Orbital emphysema is generally a benign, self-limiting condition with an excellent prognosis with regard to visual acuity (Muhammad and Simpson 1996). Nearly all reported cases of orbital emphysema with subsequent optic nerve compression showed complete recovery of visual acuity.

Epidemiology

Orbital emphysema is detected in up to 50% of orbital wall fractures on CT scan (Key et al. 2008). Very few cases of orbital emphysema with optic nerve compression have been reported.

Cross-References

- ▶ Orbital Floor Fracture
- ▶ Proptosis
- ▶ Retrobulbar Hemorrhage

References

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Incisional Biopsy

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Synonyms

Biopsy

Definition

An incisional biopsy is the partial removal of a lesion.

Purpose

To sample, diagnose, or to partially remove the lesion.

Principle

First, the tissue surrounding the lesion is anesthetized with local anesthetic with epinephrine. A scalpel or scissors are used to incise and remove a portion of the lesion, usually for histopathologic analysis. A type of incisional biopsy is the shave biopsy, where the base of a lesion is shaved flush with the skin surface. A punch biopsy is an incisional biopsy, commonly used to diagnose

lesions highly suspicious for malignancy, such as squamous or basal cell carcinoma.

Indication

An incisional biopsy is useful for the partial removal of a benign lesion, or one that is suspicious for malignancy.

Contraindication

This type of biopsy is contraindicated with any lesion already confirmed to be malignant. Abnormal bleeding times, due to therapeutic or pathological causes, may also be contraindications. Complete excision is more appropriate when incisional biopsy would create problems with structure or function (Nerad 2001; Albert and Jakobiec 2008).

Advantages/Disadvantages

One of the major advantages of this type of biopsy is that a benign lesion may be properly sampled or made cosmetically pleasing with a very minor surgical intervention. Disadvantages of this type of biopsy include the need for more surgery if the lesion is confirmed to be malignant or to require removal.

Cross-References

▶ Basal Cell Carcinoma of Eyelid
▶ Squamous Cell Carcinoma of Eyelid

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Inclusion Conjunctivitis

▶ Chlamydia

Inclusion Cyst of Conjunctival Epithelium

▶ Conjunctival Inclusion Cysts

Incomplete Achromatopsia

▶ Dyschromatopsia

Incontinentia Pigmenti (IP)

▶ Bloch-Sulzberger Syndrome (Incontinentia Pigmenti)

Increased Orbital Pressure

▶ Orbital Compartment Syndrome

Indermil

▶ Cyanoacrylate Adhesive

Indeterminate Melanocytic Lesions of the Choroid

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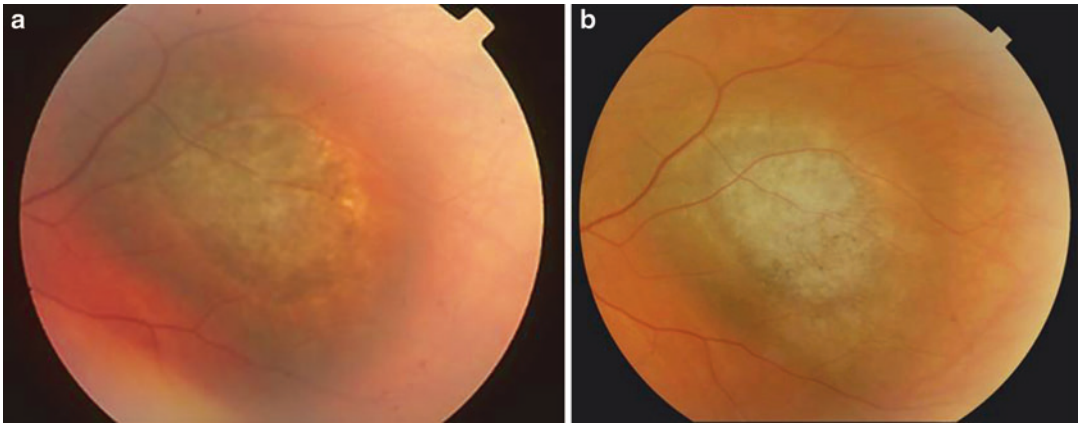
Synonyms

Suspicious pigmented choroidal lesions



Indeterminate Melanocytic Lesions of the Choroid, Fig. 1 (**A**). Patient diagnosed with a suspicious choroidal lesion. (**B**). Lesion remains stable 8 years after observation

Definition

A lesion considered to be intermediate between a nevus and melanoma that may represent a tumor with malignant potential.

Clinical Presentation

The following factors are associated with a significant increase in the risk of transformation: thickness greater than 2 mm, subretinal fluid accumulation, symptoms (decreased vision, presence of flashes), presence of orange pigment, margin touching the optic disc (Shields et al. 2000).

Diagnostics

Uveal nevi are generally flat, slate gray lesions without sharply demarcated margins and a size limited to about 6 mm in diameter. There is considerable overlap in size distributions of nevi, indeterminate lesions, and small melanomas. An observational approach for lesions less than 3 mm in height and 10 mm in diameter is common. When observation is chosen, follow-up at 6-month intervals is necessary, using fundus photography and ultrasound to identify any evidence of malignant transformation. Diagnosis can be especially difficult in borderline cases with characteristics of both lesions (Fig. 1).

Differential Diagnosis

Choroidal nevus, (small) uveal melanoma.

Therapy

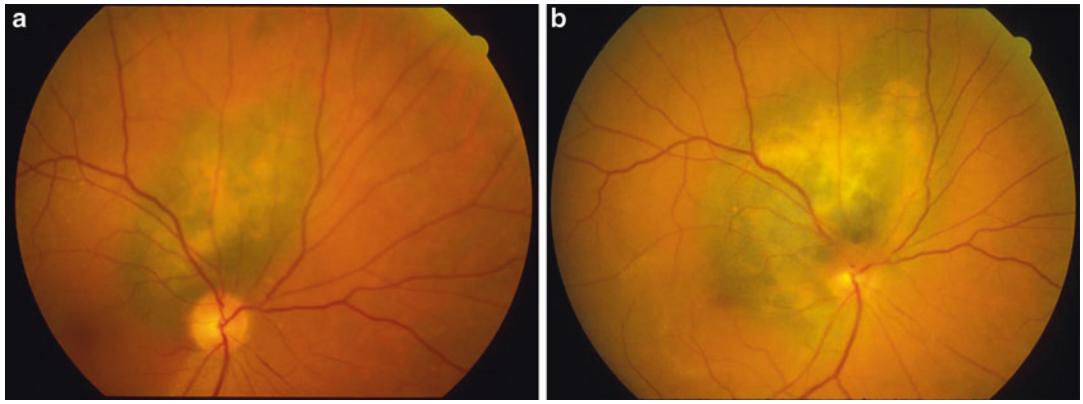
Suspicious lesions are followed closely at regular intervals. The strongest sign of malignant transformation is growth of the tumor, and treatment is recommended. Radiotherapy (brachytherapy or proton therapy) is a common treatment modality (Fig. 2).

Epidemiology

Benign nevi of the choroid are common in white populations, and the gender-specific prevalence rates are 8.9% and 8.3% for females and males, respectively (Sumich et al. 1998). Patients with indeterminate lesions are older and more likely to be female than patients with a definite melanoma. It has been estimated that 1 in 8,845 choroidal nevi will transform to a malignant tumor per year in the US white population (Singh 2007).

Cross-References

► Uveal Melanoma



Indeterminate Melanocytic Lesions of the Choroid, Fig. 2 (**A**). Patient diagnosed with suspicious lesion. (**B**). Malignant transformation was observed 20 months after the initial evaluation, and the patient was treated with proton therapy. (Modified from Lane et al. (2010) Mortality after diagnosis of small melanocytic lesions of the choroid. Arch Ophthalmol. 128:999. Reproduced by permission of the American Medical Association.)

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Indirect Ophthalmoscope

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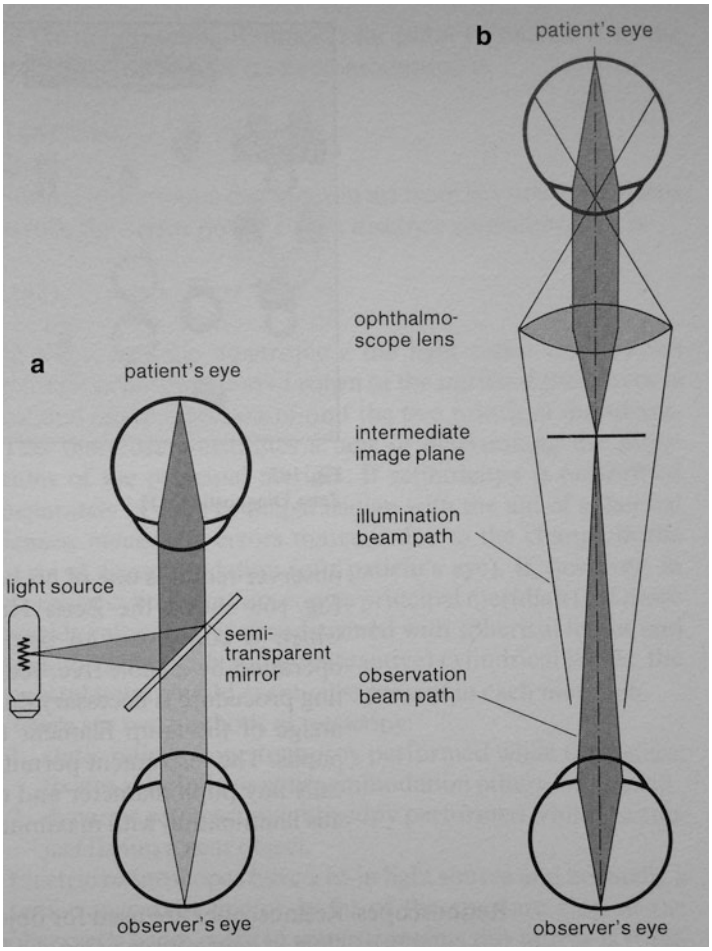
Definition

Ophthalmoscopes are used to examine the fundus of the eye. The fundus is illuminated and observed through the pupil by means of mirrors or prisms. Two different methods are used: direct ophthalmoscopy with an upright image and indirect ophthalmoscopy with an inverted image.

In direct ophthalmoscopy, the instrument is brought as close as possible to the eye. In the observation of an emmetropic eye, an upright image of the retina is obtained with a magnification of approximately 15× and a field of view of between 3° und 16°. The Recoss disk with its supplementary lenses used to compensate for ametropia can provide an initial rough estimate for the refraction of the patient's eye. In some ophthalmoscopes, it is also possible to switch a fixation target into the beam path for testing the fixation point of the retina.

In indirect ophthalmoscopy, an ophthalmoscope lens is held between the instrument and the patient's eye. This lens is then traversed by the illumination and observation beam paths at the same time. The light form the ophthalmoscope illuminator reaches the patient's eye through the usually aspheric ophthalmoscope lens in such a way that the lamp filament is imaged in the pupil. The extent of the fundus illuminated is determined by the refractive power (12–30 D) and the diameter of the ophthalmoscope lens. The light reflected off the fundus is combined by the lens to form an inverted, real image in the intermediate



Indirect Ophthalmoscope, Fig. 1 Ophthalmoscopy: (**a**) direct and (**b**) indirect

plane, where it is then viewed by the observer. The total magnification is between 2 and 5× and the field of view between 40° and 60°.

Apart from handheld ophthalmoscopes, head-worn ophthalmoscopes are also available for stereoscopic indirect ophthalmoscopy. They are mostly used for applications where the observer requires one of his hands for manipulation purposes (Fig. 1).

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Indocyanine Green

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Definition

Indocyanine green (ICG) is a tricarbocyanine dye (775 Da) with the molecular formula of $C_{43}H_{47}N_2NaO_6S_2$. Following intravenous injection, it remains 98% protein bound within the intravascular space and is an excellent tool for imaging the choroidal circulation. It is cleared by the liver without undergoing enterohepatic

circulation (Gass 1997; Guyer et al. 1999; Klais et al. 2006).

Purpose

Indocyanine green angiography is used to image the choroidal circulation during ocular angiography (Figs. 1 and 2).

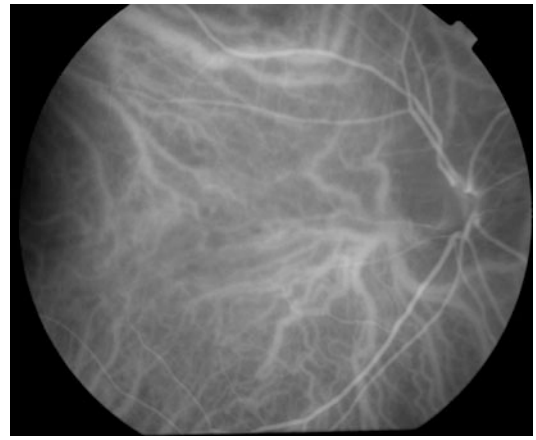
Principle

Indocyanine angiography is based on the ability of indocyanine green to absorb photons of light in the near-infrared wavelength (790–805 nm) and emit them at wavelengths greater than 825 nm. Since it remains highly protein bound in the intravascular space following intravenous administration, it is ideal for imaging choroidal vasculature and pathology. Angiographic images are captured with a fundus camera containing an outbound light filter that only transmits near-infrared light and an inbound image filter that blocks all wavelengths shorter than 825 nm.

Indication

Indications for ICG angiography include choroidal neovascular membranes, pigment epithelial detachments, polypoidal choroidal vasculopathy, retinal angiomatous proliferation, central serous retinopathy, intraocular tumors, and choroidal inflammatory conditions.

The technique of ICG angiography begins with an intravenous injection of indocyanine green dye (5 ml of 5 mg/ml solution) through a peripheral intravenous access. This is followed immediately with fundus photography using a special ICG camera fitted with appropriate outbound and inbound filters. Digital camera systems are primarily used for ICG angiography since 35 mm film-based systems have difficulty capturing weak ICG fluorescent signals at wavelengths of over 825 nm. The latest generations of ICG fundus



Indocyanine Green, Fig. 1 Indocyanine green angiography of the ocular fundus

Indocyanine Green, Fig. 2 Vial of indocyanine green dye

cameras produce high-quality images with digital subtraction software to eliminate static fluorescence and a scanning laser ophthalmoscope with high-resolution video cameras to capture real-time, high-speed images. Indocyanine green angiography can be performed simultaneously with fluorescein angiography by utilizing confocal scanning laser ophthalmoscopy and specialized filters.

Similar to fluorescein angiography, abnormalities on ICG angiography are described as either hypofluorescent or hyperfluorescent, depending on whether they appear darker or brighter than normal, respectively. Hypofluorescent abnormalities represent vascular filling defects or areas where overlying blockage from blood, pigment, or tissue limits fluorescence. Hyperfluorescent abnormalities reflect either areas with increased amounts of ICG dye or areas of increased signal transmission from ICG due to less than normal overlying blockage.

Contraindication

Indocyanine green is generally safe with less than 1% of patients suffering a mild reaction, including nausea, vomiting, or pruritus. However, isolated reports of anaphylactic shock have been described. Clinicians should always inquire about prior reactions before injecting ICG. Indocyanine green should be used with caution in patients with an iodine or shellfish allergy as ICG contains 5% iodine. Indocyanine green should likely be avoided in patients with liver failure or uremia since clearance may be compromised. Although it does not appear to cross the placenta, ICG is classified as a category C drug during pregnancy since adequate safety studies are not available.

Advantages/Disadvantages

Advantages of ICG include its great safety profile and its ability to remain within the choroidal vasculature, making it ideal for imaging choroidal pathology. Since ICG fluoresces in the near-infrared wavelengths, it can readily produce fluorescent images through various opacities, including serosanguineous fluid, hemorrhage, pigment, and lipid exudates. It can also be given before, concurrently, or following sodium fluorescein. One potential disadvantage of ICG is its low efficacy of producing a fluorescent signal (less than 4%) which requires specialized imaging platforms.

Cross-References

- ▶ Angiography, Fluorescein
- ▶ Retina, Structure of
- ▶ Retinal Blood Vessels

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Induced Retinal Toxicity

▶ Desferrioxamine Retinopathy

Infantile Glaucoma

▶ Primary Congenital Glaucoma

Infectious Keratitis with Ulceration

▶ Ulcerative Keratitis Disease

Infectious Papilloma

▶ Human Papilloma Viruses, Ocular Infection

Inferior Cantholysis

▶ Cantholysis

Inferior Tarsal Muscle

▶ Retractors, Lower Eyelid
▶ Tarsal Muscles, Inferior

Inflammatory Eye Disease

▶ Other Uveitic Etiologies

Inflammatory Optic Neuropathy

▶ Optic Neuritis: Overview

Inflammatory Pseudoguttatae

▶ Pseudoguttatae: Inflammatory Disease

Infraciliary Blepharoplasty Incision, for Anterior Orbitotomy

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Synonyms

Subciliary incision, for anterior orbitotomy

Definition

A transcutaneous orbitotomy designed to access the inferior orbital area in both the preseptal and postseptal planes.

Indications

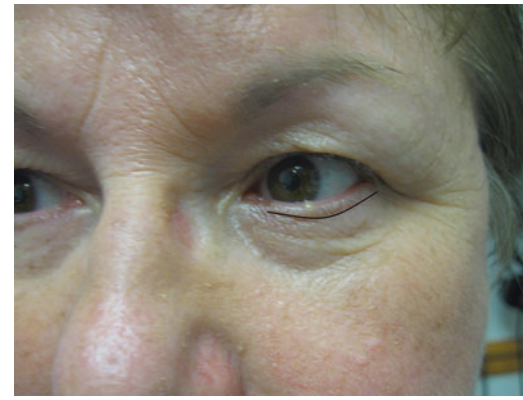
Anteriorly placed lesions or orbital fractures in the inferior orbit can be approached through multiple approaches. Traditionally, an infraciliary blepharoplasty incision has been used to approach these areas. These incisions generally heal well and are hidden in the eyelash line (Nerad 2001; Levine 2003).

Contraindication

Contraindications for patients who wish to avoid a skin incision and for patients who are not medically stable for surgery.

Techniques and Principles

A skin incision is created approximately 1–2 mm beneath the inferior eyelashes (Fig. 1). The



Infraciliary Blepharoplasty Incision, for Anterior Orbitotomy, Fig. 1 Left lower eyelid of patient marked 1–2 mm beneath the eyelash line as an infraciliary incision

incision is then carried out posteriorly to the preseptal tissues or down to the orbital rim to access the extraperiosteal area for orbital decompression, blowout floor fracture repair, etc (Nerad 2001; Levine 2003).

Outcome

Broad visualization of the inferior orbit for lesion biopsy, decompression, or orbital fracture repair.

Complications

Risks include anesthesia, bleeding, pain, infection, scarring, lower eyelid retraction, swelling, loss of vision, damage to adjacent structures, diplopia, and need for additional procedures.

Cross-References

- ▶ Anterior Orbitotomy
- ▶ Blowout Fractures
- ▶ Extraperiosteal Route
- ▶ Graves Ophthalmopathy
- ▶ Orbit, Inflammation of
- ▶ Orbitotomy
- ▶ Transcutaneous Routes

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Infraciliary Incision

- ▶ Transcutaneous Routes

Infraorbital Nerve

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Definition

The *infraorbital nerve* is solely a sensory nerve and is the distal extension of the maxillary division of the trigeminal nerve (V2). The infraorbital nerve provides sensory innervation to the skin overlying the maxillary bones and the mucosa of the maxillary sinuses. Distal to the inferior orbital fissure, the maxillary nerve becomes the infraorbital nerve and travels in the infraorbital grove and canal to exit from the infraorbital foramen and then splits into the inferior palpebral nerve and several other cutaneous nerves that serve sensation of the face.

Cross-References

- ▶ Maxillary Nerve

Further Reading

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Infrared Digital Photography

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Synonyms

Near-IR digital photography

Definition

Digital photography of ocular structures employing light of near infrared wavelength.

Purpose

To image structures of the eye without causing pupillary constriction (Dekking 1933; Kugelberg 1934).

Principle

IR rays used in ophthalmic photography and digital imaging are near-IR waves IR-A (780–1400 nm). The use of infrared light allows for imaging the pupil without constricting it and without being noticed by the subject.

Indication

Nonmydriatic fundus cameras use an IR viewing system to exploit the patient's natural dilation in a dark room. Furthermore, the technique allows evaluation of the anterior surface of the iris and near-IR subretinal imaging (Saine et al. 2006).

Advantage/Disadvantage

IR light passes easily through the cornea, sclera, and pigment epithelium.

Imaging with Indocyanine Green (ICG) which has a peak spectral absorption in the near infrared range of the light spectrum (approx. 800 nm). Light absorption and fluorescence occur within the near infrared spectrum, which allows for improved visualization through the retinal pigment, hemorrhages, and lipid and subretinal fluid (Chiang et al. 2011; Theelen et al. 2010).

Cross-References

- ▶ Indocyanine Green
- ▶ Iris Nevus Syndrome
- ▶ Retinal Pigment Epithelium

References

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Infrared Pupillographers

- ▶ Infrared Pupillometers

Infrared Pupillometers

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Synonyms

Infrared pupillographers

Definition

Infrared device for measurement of pupil diameter.

Purpose

Assessment of pupil diameter prior to refractive surgery procedures and differentiation of neuro-ophthalmological disorders.

Principle

Infrared light-emitting diodes (IR-LEDs) illuminate the eyes with long-wave light that does not affect pupil size. There are stationary digital infrared devices for binocular simultaneous measurements of pupil diameter at three illuminance levels as well as handheld infrared devices for subjective monocular pupil measurement, where the examiner estimates pupil size by a superimposed millimeter ruler Kohnen et al. 2004; Schnitzler et al. 2000.

Indication

Prior to refractive procedures, for clinical application in neuro-ophthalmology (e.g., distinguishing Horner syndrome from physiologic anisocoria) (Wilhelm and Wilhelm 2003).

Advantage/Disadvantage

Some instruments allow for recording of only one pupil at a time, whereas other devices incorporate binocular systems. Binocular dual channel pupillometers are best suited for clinical application in neuro-ophthalmology to detect possible unequal direct and consensual pupil reactions (Wilhelm and Wilhelm 2003).

Cross-References

- ▶ Glare, General
- ▶ Horner's Syndrome
- ▶ Photophobia
- ▶ Pupil Diameter
- ▶ Pupillary Light Reflex
- ▶ Refractive Surgery
- ▶ Scoptopic Pupil Diameter

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Inherited Color Vision Defects

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Synonyms

Congenital color vision defects

Definition

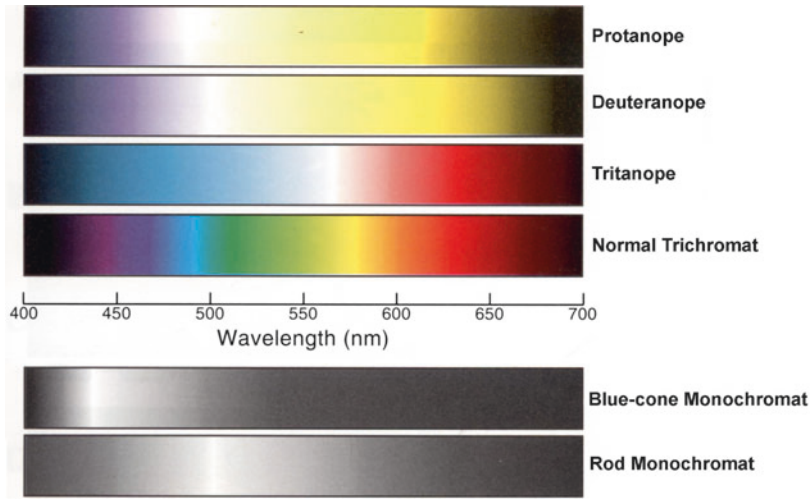
Inherited impairment in color discrimination, ranging from a complete absence of color discrimination to slightly altered color perception. Figure 1 illustrates the visual consequences of the various forms of inherited color vision defect.

Etiology

All inherited color vision defects have a genetic origin and are typically associated with disruptions in the expression of normal cone photopigments. Red-green color vision defects are caused by deletions or mutations in the X-encoded long- (L-) and middle-wavelength sensitive (M-) opsin gene array. Blue cone monochromacy is linked to a complete absence of L- and M-opsin in the retina, usually due to a deletion of cis-regulatory elements in the L-/M-opsin gene array. Blue-yellow defects are associated with mutations in the short-wavelength sensitive (S-) opsin gene on chromosome 7. Rod monochromacy has been linked to numerous mutations in *CNGA3* and *CNGB3* (which encode the α- and β-subunits, respectively, of the cone cyclic nucleotide-gated (CNG) channel), as well as *GNAT2*, which encodes the α-subunit of the cone G-protein transducin, and *PDE6C*, which encodes phosphodiesterase.

Occurrence

Inherited color vision defects have variable occurrence. Owing to their X-linked nature, red-green defects affect predominantly males, with an estimated 1 in 12 males of Western European descent manifesting some form of red-green defect. Males of Asian and African descent have a lower reported incidence. Approximately 1 in 7 females is a carrier of a red-green defect, but only 1 in 200 females manifests a red-green defect. Tritan color vision defects affect males and females equally, and the estimated incidence is around 1 in 30,000. Blue cone monochromacy is transmitted as an X-linked defect, so it selectively affects males at a rate of about 1:100,000. Affected females have not been reported in the literature, which is not surprising given the



Inherited Color Vision Defects, Fig. 1 Perceptual consequences of inherited color vision defects. Shown is a computer simulation of the color spectrum as it would appear to a protanope, deuteranope, tritanope, and normal trichromat. Each color vision deficiency shows greatly reduced chromatic discrimination compared to that of a normal trichromat. The *bottom* two panels reveal the perceptual consequences of monochromacy on the appearance of the spectrum for a blue cone monochromat and rod monochromat (Adapted and reproduced with permission of Cambridge University Press)

estimated frequency of 1 in 10 billion. Rod monochromacy is thought to affect males and females equally and the estimated prevalence is about 1:33,000.

Classification

The red/green defects can be separated based on the dimensionality of the residual color vision (dichromat or anomalous trichromat) and based on the spectral subtype of the remaining cone (protan or deutan). Individuals with an absence of L-cone function are said to have a protan defect. Protanopes are dichromats who possess an S-pigment and an M-pigment. Protanomalous trichromats possess a normal S-pigment and two spectrally distinct M-pigments. Perceptually, the absence of a cone type can have differing effects. Individuals with a protan defect are less sensitive to light in the long-wavelength (red) portion of the spectrum. Therefore, the brightness of red, orange, and yellow is reduced compared with a normal observer. Furthermore, they may have problems in distinguishing red from green, as well as difficulties differentiating a red hue from black. Individuals with an absence of M-cone function are said to have a deutan defect. A deuteranope possesses an S-pigment and an L-pigment, whereas deuteranomalous trichromats possess an S-pigment and two spectrally distinct L-pigments. Deutans suffer similar hue discrimination problems as the protans, but without the long-wavelength dimming.

Blue-yellow defects (tritanopia) are relatively rare and affect the S-cones in the retina. The ability to distinguish colors in the short- and middle-wavelength regions of the spectrum is compromised. It is important to distinguish between an inherited blue-yellow defect and an acquired defect, as many acquired color defects can arise as a consequence of a traumatic event, such as exposure to toxins, a cortical injury, or an ocular disease like glaucoma or retinitis pigmentosa.

In blue cone monochromacy, both L- and M-cone functions are absent. Since L- and M-cones comprise about 95% of the total cone population, these individuals have a severe visual impairment, including photophobia, poor acuity, minimally detectable electroretinogram (ERG) responses, and diminished color discrimination. Any residual color discrimination in these individuals is based solely on the S-cones and rods.

In rod monochromacy, all cone function is absent or severely diminished. It is typically characterized by an absolute lack of color discrimination, photophobia (light sensitivity), reduced acuity, visual nystagmus, and a nondetectable cone ERG.

Cross-References

- ▶ Achromatopsia
- ▶ Color Blindness
- ▶ Color Vision, Three Cone Opsins
- ▶ Lanthony Tritan Album
- ▶ Red-green Color Vision, Defects
- ▶ X-Linked Megalocornea

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Inherited Color Vision Disorders

- ▶ Primary Color Vision Deficiency

Inherited Cone Dysfunction

- ▶ Cone Dystrophies/Degeneration

Inherited Dyschromatopsia

► Primary Color Vision Deficiency

Inherited Macular Dystrophy

► Macular Dystrophy

Inoculation Lymphoreticulosis

► Cat Scratch Disease

Interface Fluid Syndrome

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Synonyms

IFS

Definition

Corneal edema which occurs in eyes that have had lamellar corneal refractive surgery.

Etiology

The most common cause of IFS is steroid-induced ocular hypertension. This results in transudation of fluid through the endothelium and stromal bed with tumor accumulation and swelling in the LASIK wound.

Other known causes for IFS are anterior uveitis, endothelial cell dysfunctions, or trauma.

Occurrence

Little is known about the occurrence of IFS, but due to reports of steroid response ocular hypertension between 5% and 36% in general population, it is believed that the incidence of IFS is significantly higher.

Classification

Up to today no classification for IFS has been made.

Cross-References

► Lamellar Keratoplasty

Further Reading

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Interferometry, General

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Overview

Interferometry is a technique where two or more waves, which originated from the same source but traversed different paths, are interfered in order to retrieve information about the paths travelled by

these waves. Although interference is observed for all types of waves, the technique of interferometry is usually implemented using electromagnetic waves (mostly light). Interferometry is a very broad field and quite old. The initial theories on interferometry were proposed in the seventeenth century and a variety of different interferometers have been proposed since then. In the modern times, these old interferometers have been combined with lasers and electronics to develop extremely precise measuring devices which are being used in various areas of science and technology. Major areas include optical metrology, astronomy, optical communications, spectroscopy, biomedical imaging, surface profiling, mechanical stress/strain measurements, and many more.

Basic Principle

The basic principle behind all the interferometers is the interference of light. Whenever two beams, with a defined phase relationship with each other, are superimposed, interference is observed. If the beams are in phase (i.e., peak of one wave corresponds to the peak of the other), then they add up and constructive interference is observed while when they are out of phase, (i.e., peak of one wave corresponds to the trough of the other) they cancel each other and destructive interference is observed. If the phase relationship is in between the two extreme cases, then the intensities will add up partially. Therefore, by measuring the interference pattern of two beams, the phase relationship between them can be obtained. This phase relationship can then be used to retrieve more information on the path traveled by the interfering beams.

Classification of Interferometers

Interference can be observed by division of wavefront or division of amplitude. This differentiation is commonly used to classify interferometers. The example of interference by division of wavefront is the Young's double-slit interferometer and Fresnel biprism interferometer. The example of interference by the division of amplitude includes Fizeau interferometer or Michelson's interferometer.

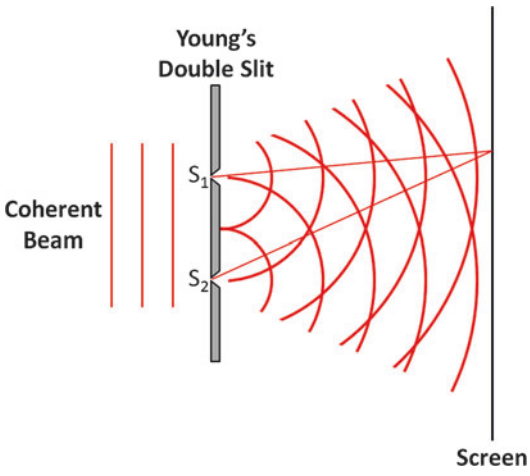
The interferometers could also be categorized based on the paths travelled by the interfering beams. Common path interferometers are the ones where the two interfering beams travel along the same path such as Sagnac interferometer or shearing interferometer, while in double path interferometer the two interfering beams travel different paths, such as Michelson's interferometer or Mach-Zehnder interferometer. Details on many of the interferometers mentioned above are provided below.

I

Common Interferometers

Young's Double Slit Interferometer

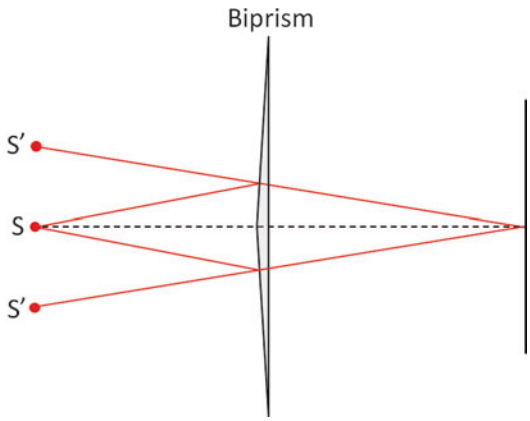
This interferometer was one of the first experiments which described the wave nature of light. A coherent light source illuminates two slits which split the wavefront of the incident light into two. The split wavefronts then interfere on the screen and generate an interference pattern. Figure 1 shows the Young's double slit interferometer.



Interferometry, General, Fig. 1 Young's double slit interferometer

Fresnel Biprism Interferometer

This is an alternative method of implementing Young's double slit configuration. One of the limitations of Young's double slit interferometer is that too little light passes through the two slits to observe interference. This interferometer uses Fresnel biprism to split the wavefront efficiently thus increasing the contrast of interference pattern. The apparatus is shown in Fig. 2. Fresnel biprism has a very small refracting angle; therefore, when the light from a coherent point source is made incident on the Fresnel biprism, it splits the wavefront into two. On the screen it appears that there are two point sources, one each for each split wavefront. These two wavefronts interfere on the screen to generate the interference pattern.



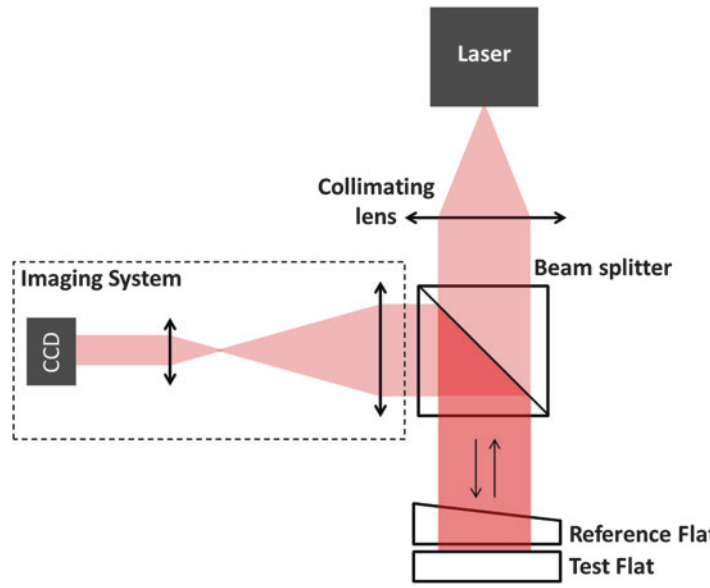
Interferometry, General, Fig. 2 Fresnel biprism interferometer

Fizeau Interferometer

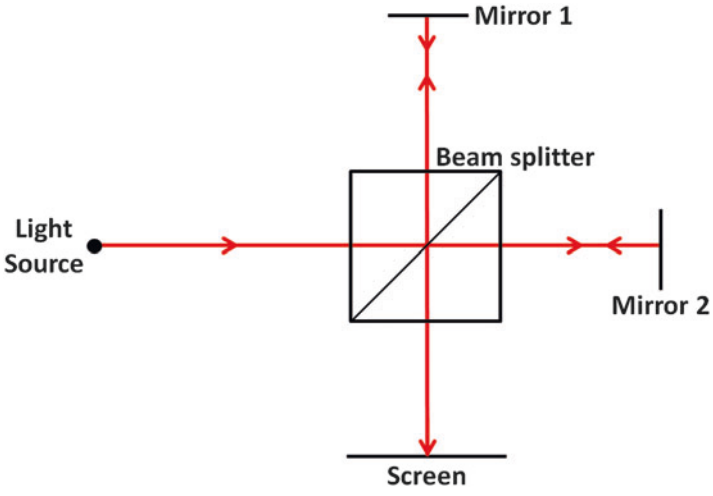
In a Fizeau interferometer, a collimated beam is made incident on two flat surfaces separated by an air gap. The light reflected from the two flat surfaces interfere to generate the fringes of equal thickness. If the flatness of one surface is established (reference flat), then the flatness of the other surface (test flat) can be evaluated on the basis of the fringes of equal thickness. Figure 3 shows the schematic of a Fizeau interferometer, where the reference flat is kept on top of the test flat. Convex and concave surfaces can also be evaluated by Fizeau interferometer by using a converging or diverging beam. Since the two interfering beams are formed by splitting the entire wavefront, this is an interferometer which is based on interference by division of amplitude.

Michelson Interferometer

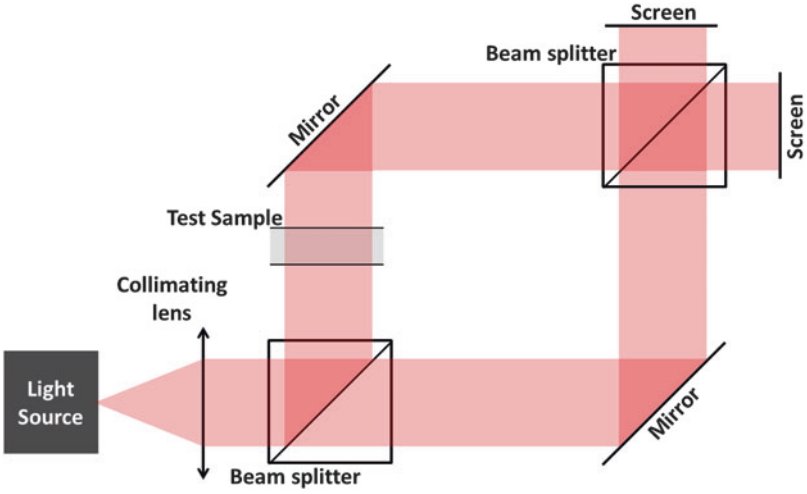
The schematic of the Michelson's interferometer is shown in Fig. 4. Light beam from a light source is split into two beams using a beamsplitter. The



Interferometry, General, Fig. 3 The schematic of Fizeau interferometer



Interferometry, General, Fig. 4 The schematic of the Michelson's interferometer



Interferometry, General, Fig. 5 Schematic of Mach-Zehnder interferometer

two beams are made incident on two mirrors, one reference and other test mirror. Light reflecting back from the two mirrors interfere on the screen. Effectively the interference is observed between the reflections of the light source from two mirrors.

Optical coherence tomography (OCT) is a fiber-based Michelson's interferometer where the test mirror is replaced with the sample. Based on the interference pattern, the information of the sample is obtained.

Mach-Zehnder Interferometer

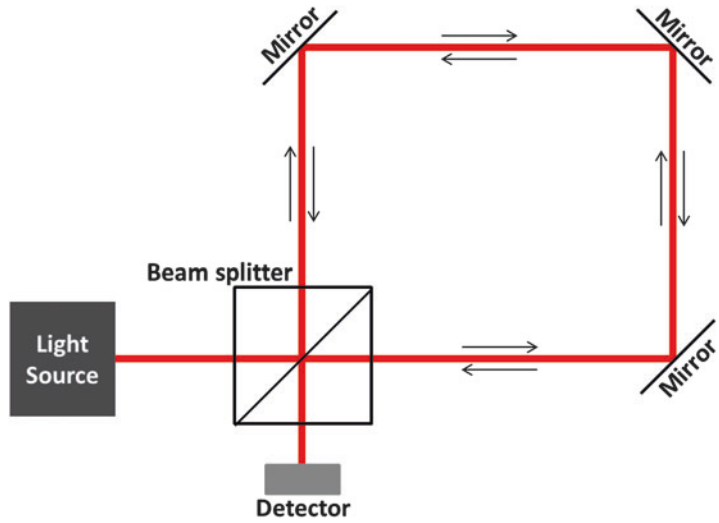
In Mach-Zehnder interferometer, the light from a coherent point source is first collimated by a lens and then split into two paths using a beamsplitter (Fig. 5). In one of the paths, a test sample is placed, while the other path is used as reference. The light from the two paths is then overlapped to interfere the two beams. Based on the interference pattern, the phase shift introduced by the test sample is measured which can then be used to retrieve other physical properties of the sample.

Sagnac Interferometer

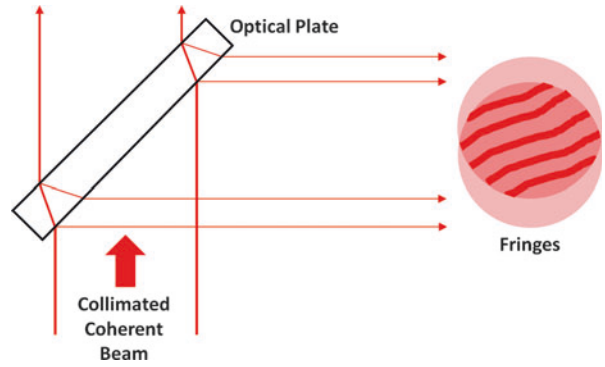
Sagnac interferometer is widely used to measure rotation. In this interferometer, light from a coherent light source is split into two using a beamsplitter. The spit beams are made to travel in the opposite directions along the same path as shown in Fig. 6. Depending on the angular velocity of rotation of the interferometer, phase of the beams traveling in the opposite directions is modified causing a shift in the interference pattern. Measuring this shift provides a measure for angular velocity of rotation.

Shearing Interferometer

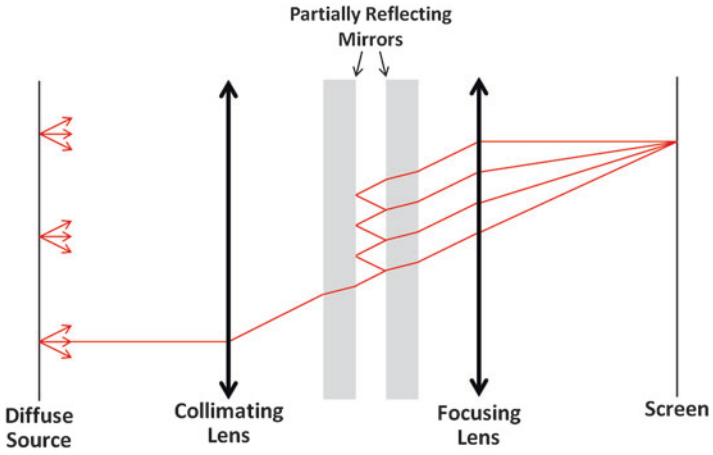
Shearing interferometer is probably the simplest type of interferometer. It consists of an optical plate with extremely flat surfaces, which are slightly wedged with respect to each other. A collimated beam is made incident at 45° on this plate (Fig. 7). The beam reflects from the two interfaces and interferes. Due to the finite thickness of the optical plate and the wedge between the two surfaces, the two beams are separated laterally, hence the name shearing interferometer. The interference is observed only in the



Interferometry, General, Fig. 6 Schematic of Sagnac interferometer



Interferometry, General, Fig. 7 Schematic of the shearing interferometer



Interferometry, General, Fig. 8 Schematic of the Fabry-Perot interferometer

region where the two reflected beams overlap. Most common application of shearing interferometer is to measure the collimation of the laser beams as the interference pattern is only observed if the incident beam is collimated.

Fabry-Perot Interferometer

The Fabry-Perot interferometer consists of two partially reflecting mirrors, which reflect light towards each other thus making an optical cavity. These mirrors are usually separated from each other by several millimeters. In a traditional configuration of Fabry-Perot interferometer, a diffuse light source is used to illuminate the interferometer. A collimating lens collimates the light coming out of a diffuse source. The collimated light enters the cavity and gets reflected from the partially reflecting mirror multiple times, as shown in Fig. 8. Some portion of the light is transmitted at each reflection. This transmitted light is focused onto the screen using a focusing lens. Depending on the thickness of the cavity and the reflectivity of the two partially reflecting surface, a concentric interference pattern is observed on the screen.

White Light Interferometer

White light interferometers as the name suggest use broadband light sources (white light sources). Due to the broadband characteristic of these light sources, the light emitted by them has a small coherence length. Here coherence length is the distance over which the phase relationship of the beam is maintained. Therefore to observe interference, the optical path lengths of the two interfering beams should be matched within the coherence length. White-light interferometers use this phenomenon to extract information from the interference pattern. For a Michelson's interferometer (Fig. 4) with a white-light source, the interference will be observed only if the optical path lengths for the two mirrors is matched to within the coherence length. If one of the mirrors is moved axially, then on the screen the interference will only be observed when the moving mirror is at the position where the path lengths for the two mirrors match. This hence could be used to extract the position of the second mirror.

Interferometry is a broad field; in this essay, we have covered just the basics of interferometry and talked about the most common interferometers. There are many other types of interferometers that have not been discussed. To learn more, please refer to dedicated textbooks on interferometry mentioned in the references.

Cross-References

▶ Optical Coherence Tomography

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Interlenticular Opacification

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Synonyms

Interpseudophakic opacification; Interpseudophakos Elschnig pearls; Red rock syndrome

Definition

Formation of an opacifying membrane between piggyback intraocular lenses and ingrowth of proliferative crystalline lens material. The major symptom is a decrease in best-corrected visual acuity (BCVA) with a blurred vision and glare. The currently advised therapy consists of the removal of the piggyback IOL and exchange with a single IOL.

Histology

After explantation of piggyback posterior chamber intraocular lenses because of opacification between the lens optics, histopathological examinations showed retained and proliferative lens epithelial cells mixed with lens cortical material in the peripheral interface between the lenses.

Immunohistochemistry

No references in literature.

Electron Microscopy

Scanning electron microscopic photographs obtained from the posterior surface of the anterior lens, the presence of multiple small globules is observed at the midperipheral area.

Molecular Diagnostics

No references in literature.

Differential Diagnosis

- After cataract
- Sicca-Syndrom
- Lens luxation
- Imperfect refractive outcome
- Capsular block syndrome

Cross-References

▶ After Cataract
▶ Cataract Surgery
▶ Intraocular Lens

Further Reading

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Internuclear Ophthalmoplegia

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Definition

An internuclear ophthalmoplegia (INO) is a disorder of conjugate horizontal gaze. When a patient with INO is asked to move their eyes horizontally, the eye contralateral to the gaze direction will be unable to adduct, and the eye ipsilateral to the gaze direction will demonstrate a horizontal, dissociated, abducting nystagmus. For example, a right INO will present with left eye dissociated abducting nystagmus and an impairment in the ability of the right eye to adduct upon gaze to the left.

Etiology

INO is caused by damage to the medial longitudinal fasciculus (MLF), a fiber tract that extends from the rostral midbrain to the spinal cord. The MLF contains many important tracts including the pathway connecting the abducens nucleus and oculomotor nucleus, which is important for coordinating the eyes during horizontal conjugate. For example, a patient with right INO will have damage to the right MLF, preventing communication between the left abducens nucleus and the right oculomotor nucleus. As the patient tries to look to the left, the left eye will abduct, but the right eye will remain stationary. In addition, the left eye will demonstrate horizontal nystagmus due to cortical eye movement control centers attempting to compensate for the lack of adduction of the right eye.

Occurrence

INO can be caused by many conditions including multiple sclerosis (MS), brain stem infarction, tumors, arteriovenous malformations, Wernicke encephalopathy, and encephalitis. INO ranges from a mild form where the adducting eye moves slower than normal resulting in transient diplopia to a severe form where there is constant diplopia upon lateral gaze. In a young patient with a bilateral INO, one would suspect MS, whereas in an older patient one would instead suspect brain stem infarction. There may be a concomitant exotropia in patients with unilateral or bilateral INO leading to a "wall-eyed" monocular INO (WEMINO) or bilateral INO (WEBINO).

Classification

None.

Cross-References

▶ Diplopia in Vertebrobasilar System Disease
▶ Efferent Visual System (ocular motor pathways)
▶ One-and-a-Half Syndrome
▶ WEBINO ("Wall-Eyed" Bilateral Internuclear Ophthalmoplegia) Syndrome

Further Reading

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Interpseudophakic Opacification

▶ Interlenticular Opacification

Interpseudophakos Elschnig Pearls

▶ Interlenticular Opacification

Interstitial Keratitis

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Synonyms

Nonulcerative keratitis; Syphilitic keratitis

Definition

A nonsuppurative (nonmelting) inflammation of the corneal stroma that tends to spare the epithelium and endothelium.

Etiology

Many infective, immunologic, and environmental factors could contribute to this disease. Among the most common etiologic factors are syphilis and herpes viral infections. Other causes include tuberculosis, leprosy, Lyme disease, brucellosis, leptospirosis, influenza, mumps, onchocerciasis, *Acanthamoeba*, leishmaniasis, measles, *vaccinia*/*variola*, sarcoidosis, contact lens keratitis, lymphoma, and exposure to gold or arsenic. An idiopathic form of this disease is called Cogan's syndrome.

Occurrence

The ocular involvement could be seen unilaterally or bilaterally. Additionally, it could range from restricted to wide spread of the cornea. The occurrence of systemic symptoms could vary based on the underlying cause of the disease. Finding the etiologic factor is essential in treating both ocular and systemic conditions.

Classification

During the acute phase of the disease, nonspecific symptoms and signs could be seen in other forms of keratitis which include redness and tearing of the eye, pain, and photophobia followed by new vascular formation of the stoma. However, the late phase that characterizes the interstitial keratitis shows scarring that commonly leads to corneal thinning and empty ghost vessel. The differentiation of the underlying cause could be contributed to the pattern of ocular and stromal involvement, vasculature formation, and associated ocular and systemic findings.

Cross-References

▶ Cogan Syndrome
▶ Human Herpes Virus
▶ Syphilis: Overview

Further Reading

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Intracameral Antibiotics

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Definition

Administration of antibiotic agents into the anterior chamber of the eye.

Indication

Prophylaxis of postoperative endophthalmitis, therapy of fungal keratitis.

Contraindication

Allergy against applied antibiotics.

Use and Dosage

Intracameral antibiotics are applied as bolus injection into the anterior chamber at the end of cataract surgery. According to a multicenter study, administration of cefuroxime (1 mg in 0.1 ml saline) resulted in a fivefold decrease in the risk for total postoperative endophthalmitis. Other antibiotics such as cefazolin have also been applied for the prevention of postoperative endophthalmitis. For the treatment of fungal keratitis, application of intracameral amphotericin B (10 μg/0.1 mL) has shown a beneficial effect in smaller case series.

Adverse Reactions

Inadequate chemical preparation of intracameral antibiotics might result in toxic anterior segment syndrome.

Interactions

Not assessed

Cross-References

▶ Cataract Surgery
▶ Cefuroxime
▶ Fungal Keratitis with Ulceration
▶ Toxic Anterior Segment Syndrome

Further Reading

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Intradermal Nevus

▶ Nevus, Intradermal

Intraepidermal Carcinoma

▶ Bowen's Disease

Intraepithelial Epithelioma

▶ Carcinoma In Situ, of Conjunctiva

Intraocular Gases

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Synonyms

Gas tamponade; Perfluoroethane (C2F6); Perfluoropropane (C3F8); Pneumatic retinopexy; Sulfur hexafluoride (SF6)

Definition

A surgical technique involving the introduction of gases into the vitreous cavity. The gases are used either in their pure form or as a mixture with air, exploiting their different longevity and expansile properties for achieving an effective internal tamponade.

Indication

Retinal detachment surgery with vitrectomy, pneumatic retinopexy, retinal detachment surgery with scleral buckle, macular hole surgery, displacement of subretinal hemorrhage, and post-vitrectomy gas exchange.

Contraindication

Air travel within the time frame of the gas's intravitreal longevity.

Nitrous oxide use during general anesthesia (should be discontinued for at least 15 min prior to intraocular gas injection, to avoid interference in the desired bubble volume).

Techniques and Principles

In this technique the vitreous is filled with a gas bubble for the purpose of restoring the anatomy by re-opposing the retina to the underlying retinal pigment epithelium and choroid. In daily practice, air, sulfur hexafluoride (SF6), perfluoroethane (C2F6), and perfluoropropane (C3F8) are most commonly used.

The main functions of a gas bubble inside the eye are to: (1) provide internal tamponade, (2) flatten the folded retina, (3) enable visualization, (4) replace globe volume, and (5) reduce intraocular currents. Providing internal tamponade for retinal detachments has been the main indication of intraocular gas use. The purpose is to appose the break by utilizing the surface tension of the bubble. The tamponade bubble also acts to seal the break and prevent cellular elements from escaping from under the retina into the vitreous cavity, thus preventing proliferative vitreoretinopathy.

The choice of gas is sometimes based on the availability of gases and the surgeon's experience and preferences. In general, the choice of gas is dependent on the intended duration of tamponade. For simple cases where duration required is short, air could be used. In more complicated cases where longer tamponade is desired, nonexpansile concentration of gas/air mixture (18% SF6 or 14% C3F8) could be used. When a larger bubble is needed, a gas/air mixture with an expansile concentration could be used. A larger bubble has the advantage of being able to unroll the folded retina. Taken together, a clear understanding of the properties of available gases is important to making the right choice for different circumstances.

Intraocular gas injection technique in vitrectomy for retinal detachments is briefly as follows: following full vitrectomy and relieving of tractions, fluid-air exchange is used to flatten the retina, at which point endolaser can be performed. Finally, air-gas exchange is performed.

In pneumatic retinopexy careful patient selection is important, as failure of apposing the retina may subject the patient to further operations. This is an office procedure and can be performed with topical, subconjunctival, or retrobulbar

anesthesia. Gas is then injected transconjunctivally through the pars plana, frequently followed by anterior chamber paracentesis to counter the increase in intraocular volume. A variety of intraocular gases may be used (e.g., air, SF6, C3F8). In practice, 0.3 mL of 100% C3F8 is used most commonly. In cases where apposition is doubtful, subretinal fluid persists, or new breaks were found, a reoperation with either scleral buckling or vitrectomy approach is indicated.

In macular hole surgery, classically intraocular gas tamponade is injected followed by facedown posture for 1 week. This provides a mechanical effect by the buoyancy force of the bubble over the macular hole, in order to assist closure. The injecting technique is identical to that in retinal detachment surgery with vitrectomy approach. Nevertheless, the duration of postoperative posturing has been a topic of debate in recent years.

Pneumatic displacement of subretinal blood clot has been found to be therapeutic in treating polypoidal choroidal vasculopathy, macroaneurysm, choroidal neovascularization, and trauma. It has been shown to allow speedier recovery of vision and may potentially reduce the harmful effect of blood on the photoreceptors. The original procedure was to treat within 1 week from onset of hemorrhage, coupled with tissue plasminogen activator (tPA) injection. There are recent reports showing similar effects without the use of tPA and also of variable duration from onset of up to 30 days. Prior to injection, careful patient selection should be done. Distinction between subretinal blood and intraretinal blood should be made. Injecting gas for intraretinal blood will not displace the clot, but rather increases the chances of blood diffusing into the vitreous.

Postvitrectomy gas exchange may be utilized for recurrent detachment and may avoid the need for reoperation. A fluid-gas exchange could be performed at the slit lamp, using a 30-gauge needle connected to a syringe filled with the desired gas of injection. If the patient is aphakic, the procedure could be performed by inserting the needle into the anterior chamber through the cornea, instead of the pars plana approach.

Outcome

After injection, the gas bubble inside the eye undergoes three phases before complete resorption: expansion, equilibration, and dissolution. This occurs when pure expansile gases (i.e., SF6, C2F6, and C3F8) are injected (i.e., air does not expand).

The time taken for complete resorption of the bubble also depends on other factors such as lens status, aqueous turnover, presence of vitreous, presence of epiretinal membranes, ocular blood flow, and ocular elasticity. The life span of SF6 and C3F8 may be more than twice as long in aphakic nonvitrecomized eyes than in aphakic vitrectomized eyes.

Proper apposition of the break is only ensured by proper posturing of the head. This is done by assuming a facedown or prone posture immediately after surgery such that the break is located at the uppermost part of the eye and in direct contact with the bubble. Another potential advantage of facedown posturing is that this reduces the contact between the posterior surface of the lens in aphakic patient with the gas bubble and reduces the risk of cataract development. If facedown or prone posture is difficult or the patient needs to take rest from prolonged facedown position, lying laterally on the opposite side of the break is also acceptable (i.e., lying on the left for a right side break). This could be facilitated with the use of pillows designed for posturing purposes. As chorioretinal adhesion from laser or cryotherapy requires up to 14 days to become effective, the patient's compliance should be reassured and monitored. Vision is usually poor during the life span of the bubble, mainly due to diffraction and glare.

Complications

Breakup of the gas bubble into a few smaller bubbles (i.e., "fish eggs") by poor injection techniques, resulting in ineffective tamponade/therapeutic effect.

In case PVR has already set in, gas injection may be complicated by formation of new retinal breaks or extension of existing breaks, which usually occur at the edge of laser marks.

Gas-induced cataract, usually in the form of feathery posterior subcapsular cataracts.

Raised intraocular pressure is more frequent when expansile gases or gas/air mixtures of high purity are used. A 26–59% incidence was reported.

Gas leakage from sclerotomies can result in hypotony. Choroidal effusion or hemorrhage may occur with prolonged hypotony.

Migration of gas into the subretinal space can occur both intraoperatively and in the postoperative period at which point it may cause re-detachment.

In aphakic eyes or in pseudophakic eyes with a nonintact posterior capsule, gas may migrate into the anterior chamber. Prolonged contact of the bubble with the corneal endothelium may predispose it to hypoxia and decompensation.

With combined phacovitrectomy and intraocular gas injection, the intraocular lens (IOL) may be pushed forward into the anterior chamber, causing optic capture.

Cross-References

► Pneumatic Retinopexy
► Retinal Detachment

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Intraocular Infection

► Endophthalmitis

Intraocular Injection

► Intravitreal Injections

Intraocular Injection of Ocular Drugs

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Indications

Intraocular injections are the fastest growing procedure in ophthalmology. They are commonly used for the treatment age-related macular degeneration (bevacizumab, ranibizumab), iris neovascularization secondary to proliferative diabetic retinopathy (bevacizumab), and macular edema (bevacizumab and triamcinolone acetonide) due to diabetic retinopathy, vein occlusion, or uveitis.

In addition intravitreal methotrexate has been used to treat intraocular lymphoma associated with primary central nervous system lymphoma. Less commonly it has been used in patients with uveitis and advanced proliferative diabetic retinopathy.

Adverse Effects

Intravitreal injections often lead to increased intraocular pressure (IOP) immediately after the procedure. In 2008, Kim et al. demonstrated that eyes injected with ranibizumab, bevacizumab, pegaptanib, and triamcinolone acetonide had transient IOP spikes immediately after the procedure. However, close monitoring is necessary especially in patients with a history of glaucoma, ocular hypertension, or patients that are glaucoma suspects.

Other potential adverse effects include endophthalmitis, intravitreal hemorrhage, cataract, and irreversible loss of visual acuity.

Intraocular Large B-Cell Lymphoma

► Intraocular Lymphoma

Intraocular Lens

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Synonyms

IOL

Definition

Artificial lens made of transparent plastic, silicone, or acrylic that is implanted in the eye and performs in focusing images.

Epidemiology

According to industry data, the worldwide number of implanted IOLs is estimated at between six and ten million a year. The number of cataract operations per one million people per year (cataract surgery rate, CSR) varies highly from one country to another: according to the World Health Organization, the CSR is 4000–5000 in the USA and in Europe but only about 3000 in semi-industrialized countries such as India and as low as 200 in some Third World countries.

History

On November 29, 1949, Sir Harold Ridley implanted the first IOL in a human eye at St. Thomas' Hospital in London, UK. Operating microscopes did not exist at the time so a flashlight held by Ridley's nurse Ms. Clarke provided lighting for the surgery. A planned primary extracapsular procedure was performed using a large incision to implant the IOL in a human eye. Sixty years later, cataract surgery has been transformed into a highly specialized procedure with sub-2.0 mm incision surgery using ultrasound energy, even femtosecond laser technology and foldable IOL materials. The tremendous changes in IOL technology have led surgeons to use today's spherical, aspheric, multifocal, and toric IOL to correct not only aphakia but also astigmatism, higher-order aberrations, and presbyopia (Kohnen and Koch 2009; Kohnen et al. 2009).

Clinical Features

There are four different basic types of IOL:

- Monofocal (also known as standard IOL)
- Multifocal
- Accommodative
- Toric

Each of these types can have additional attributes like asphericity or blue-light filtering. See also section "Cross-References" list below displaying different types of IOL.

Tests

During the decades, IOL have undergone extensive research and testing in Europe, Asia, and the USA and have been proven safe for the treatment of cataracts and refractive errors.

Differential Diagnosis

Clinical aspects of an IOL with its optics and haptics clearly identify an IOL if the quality of the optical media, especially the cornea, is not reduced significantly. Rarely, a silicone bubble after vitreoretinal surgery on the posterior surface of an IOL may be mistaken for a dislocated IOL.

Etiology

See also section "Clinical Features."

Treatment

See also entries "▶ Cataract Surgery" and "▶ Refractive Surgery" describing different IOL implantation techniques.

Cross-References

- ▶ Accommodative Intraocular Lens
- ▶ Acrylic Intraocular Lens
- ▶ Artisan Lens
- ▶ Cataract Surgery
- ▶ Collamer Intraocular Lens
- ▶ Foldable Intraocular Lens
- ▶ Hydrophilic Acrylic Intraocular Lens
- ▶ Hydrophobic Acrylic Intraocular Lens
- ▶ Multifocal Intraocular Lens
- ▶ Phakic Intraocular Lens
- ▶ Photochromic Foldable Intraocular Lens
- ▶ Piggyback Intraocular Lens
- ▶ Plate-Haptic Posterior Chamber Intraocular Lens
- ▶ PRL Phakic Intraocular Lens
- ▶ Refractive Surgery
- ▶ Silicone Intraocular Lens
- ▶ Spherical Intraocular Lens
- ▶ Verisyse Iris-Supported Phakic Intraocular Lens

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Intraocular Lens Haptics

▶ Haptic

Intraocular Lymphoma

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Synonyms

Intraocular large B-cell lymphoma; Primary intraocular lymphoma; Reticulum cell sarcoma (old)

Definition

Vitreoretinal lymphoma (VRL) is a rare, mostly high-grade B-cell malignancy which can be considered a subset of primary central nervous system lymphoma (PCNSL).

Etiology

The etiology of VRL is unclear. It occurs in approximately one-quarter of patients with PCNSL. As the central nervous system, the intraocular structures lack lymphatics and lymph nodes, and the lymphoma in these cases is probably from an abnormal clone(s) of lymphocytes that is unique to immunoprivileged organs (CNS, eye,

testes) that home into the eye. Most cases of vitreoretinal lymphoma occur in immunocompetent patients. T-cell lymphoma rarely occurs. VRL is the most common type of intraocular lymphoma (Chan and Gonzales 2007; Sagoo et al. 2014).

Clinical Presentation

VRL in most cases is a disease of adults, peaking in the sixth decade, although it is diagnosed also in younger patients in the third and fourth decades. It may be monocular but is more commonly a bilateral disease, although may be asymmetrical in severity. The hallmark of VRL is the presence of cells in the vitreous, often in clumps or sheets, which is often misdiagnosed as a nonresponsive uveitis, and white-yellow retinal and subretinal infiltrates. The optic nerve head can be involved. In 80–90% cases, it appears in patients with PCNSL. The intraocular involvement occurs in approximately one-quarter of patients with PCNSL and can appear before, concomitant with, or even years after the CNS lymphoma.

Differential Diagnosis

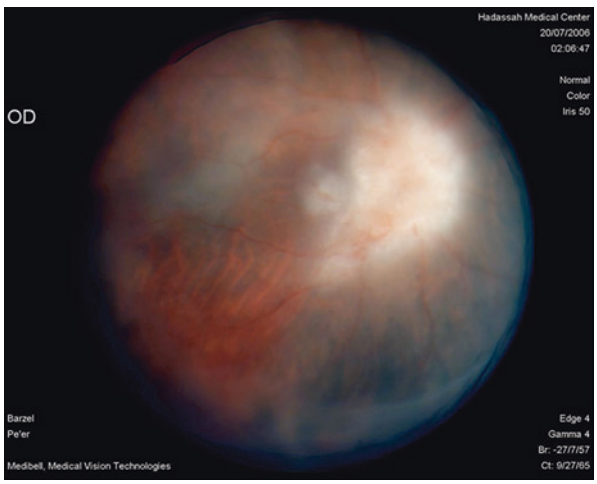
Differential diagnosis includes → all causes of posterior uveitis → noninfectious retinitis and chorioretinitis → infectious retinitis or chorioretinitis → infiltrating choroidal lesions such as metastatic tumors.

Prophylaxis

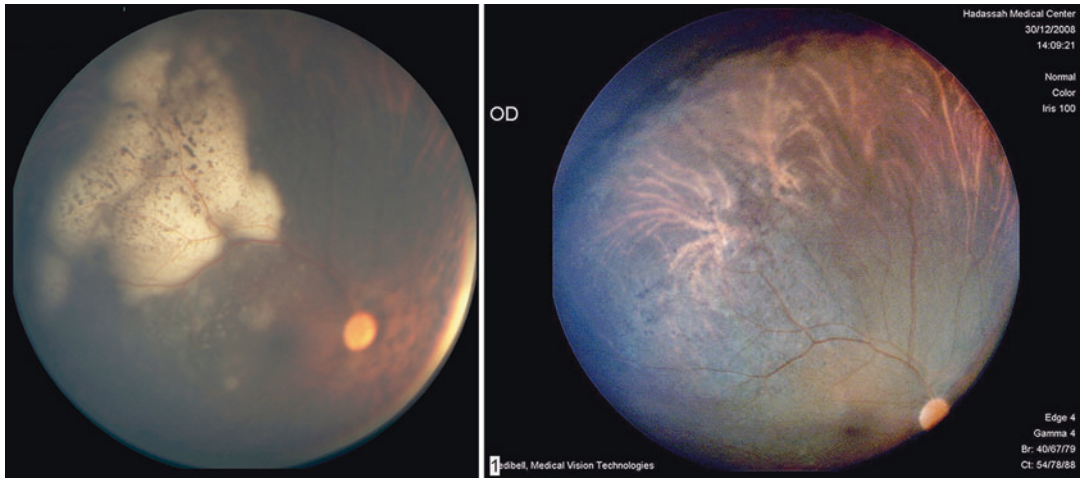
All patients with known PCNSL should be followed up routinely by an ophthalmologist to rule out ocular involvement. Early diagnosis can prevent loss of vision.

Therapy

Radiation therapy alone to the eye, with or without whole-brain radiotherapy, is still practiced in many centers. Systemic or intrathecal chemotherapy alone or in combination with radiation therapy have been used extensively. Because of limited intraocular penetration of drugs administered systemically, and side effects of systemic chemotherapy and radiation, intravitreal chemotherapy – mostly using methotrexate – has become popular since the mid-1990s with excellent local disease control. More recently, biological treatment with intravitreal injections of rituximab with or without methotrexate have been used with good results (Pe'er et al. 2009).



Intraocular Lymphoma, Fig. 1 Fundus photography shows "clouds" of lymphoma cells in the vitreous, and white infiltration of lymphoma in the retina around the optic nerve head



Intraocular Lymphoma, Fig. 2 Fundus photography shows infiltrates of lymphoma cells in the upper part of the retina with early infiltration in the macular area before treatment with intravitreal methotrexate (left) and complete disappearance of the infiltrates after treatment (right)

Prognosis

Vitreoretinal lymphoma is an intraocular disease which is not fatal, but which often accompanies PCNSL which is often fatal. The prognosis for vision depends upon the extent of the disease and the time of diagnosis. A late diagnosis can lead to visual loss, while early diagnosis and treatment can save vision.

Epidemiology

Vitreoretinal lymphoma is a rare disease which involves 20–25% of patients with PCNSL. The incidence of PCNSL is increasing and is currently ranging between 2.5 and 5 per million person-years in the immunocompetent population and is much higher in patients with AIDS (Figs. 1 and 2).

Cross-References

► Retinitis

References

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Intraocular Melanoma

► Uveal Melanoma

Intraocular Pressure

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Synonyms

IOP

Definition

The intraocular pressure is the pressure within the eye which is determined by aqueous production

and aqueous outflow from the eye. The normal range of IOP is 8–21 mmHg.

Basic Characteristics

The rate of aqueous production is defined by the Goldmann equation as follows: $PO = (F/C) + PV$, where PO is IOP, F is the rate of aqueous formation, C is the facility of outflow, and PV is the episcleral venous pressure (Alward 2000). Elevated intraocular pressure results from a decrease in facility of outflow or an increase in episcleral venous pressure.

There exists diurnal variation of IOP, typically being highest in the early morning and lowest in the late evening, though this is variable (Allingham et al. 2005).

References

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Alward LM (2000) Glaucoma: the requisites in ophthalmology. Mosby, St. Louis

Intraoperative Floppy-Iris Syndrome

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Synonyms

IFIS

Definition

Intraoperative complication during cataract surgery presenting as flaccidity of the iris is caused by lack of tension of the dilatator muscle. It is associated with the intake of selective α_{1A} adrenergic receptor blockers such as tamsolusin or doxazosin. Intraoperatively, the pupil often dilates poorly or constricts prematurely. The iris is likely to prolapse through the incision or paracentesis and shows a flaccid behavior like billowing and fluttering. IFIS can give rise to intraoperative complications such as iris aspiration and posterior capsule rupture. This phenomenon can be explained by the blocking of α_1 receptors by the drug with subsequent atrophy of the musculature. Up to now, no specific dose–response curve could be established. A preoperative washout period of at least 1 week did not have effect in most cases (Chang and Campbell 2005; Narendran et al. 2009).

Histology

Eyes with a history of tamsolusin use showed a significantly decreased thickness of the iris dilatator muscle. The iris stroma did not seem to be affected (Santaella et al. 2010). To date, there are no reports of immunohistochemistry or electron microscopy features in eyes with intake of α_{1A} adrenergic receptor blockers.

Molecular Diagnostics

No molecular diagnostics are required for diagnosis of IFIS.

Differential Diagnosis

Iris dilatator atrophy due to other reasons can have a similar intraoperative appearance.

Cross-References

► Cataract Surgery

References

Chang DF, Campbell JR (2005) Intraoperative floppy iris syndrome associated with tamsulosin. J Cataract Refract Surg 31:664–673

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Intraorbital Foreign Body (IOFB)

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Definition

Foreign body of the orbit.

Epidemiology

True epidemiologic data is unavailable due to the relatively uncommon nature of this phenomenon. Recent retrospective consecutive case series show that the majority of patients are young males, perhaps owing to the accidental and sometimes violent nature of these injuries.

Etiology

Penetrating eyelid and orbital trauma.

History

Most patients present at the time of injury. Delayed presentation may occur after seemingly trivial trauma. In these cases, patients may complain of a progressive orbital mass, signs of orbital inflammation and infection, pain on eye movements, diplopia, and/or lagophthalmos. In children or noncommunicative patients, a high index of suspicion must be maintained as this information cannot be elicited.

A thorough history directs clinical management. Mechanism of trauma, associated injury, and loss of consciousness are vital, as they provide clues to the presence of potentially life-threatening injuries. Past medical and ocular history aids in the assessment of premorbid visual function and visual rehabilitative potential.

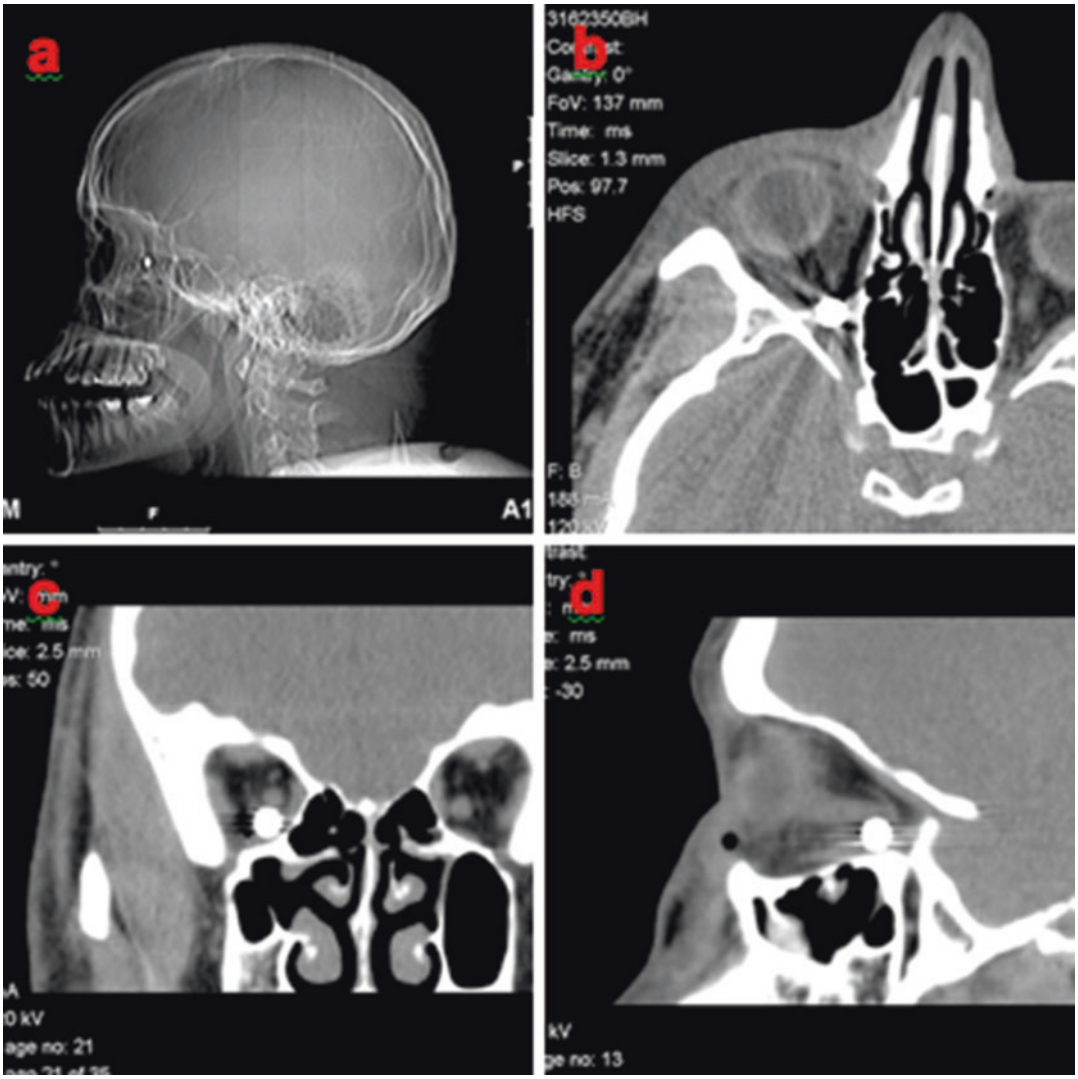
Mechanisms of trauma can broadly be grouped into blunt, sharp, and high-velocity categories. The latter two categories are more likely to result in deeper, penetrating injury. Determining the composition of the foreign body is important, as this information will greatly affect the choice of diagnostic imaging and further management.

Clinical Features

Clinical presentation varies. Decreased vision typically occurs at the time of injury. Gross ophthalmologic exam may reveal diplopia, pain with eye movements, and ophthalmoplegia. An afferent pupillary defect may be present in cases with associated traumatic optic neuropathy or orbital compartment syndrome (i.e., hemorrhage, cellulitis) (Patel et al. 2008).

On external exam, eyelid edema, ecchymoses, and lid laceration are usually present. In the absence of these findings, more subtle signs such as ptosis or lagophthalmos may be noted. Proptosis may manifest secondary to orbital hemorrhage or cellulitis. Parasthesias, point tenderness, subcutaneous emphysema, and step-off orbital rim defects may signal the presence of an orbital fracture.

On slit lamp examination, evidence of anterior segment trauma may include subconjunctival



Intraorbital Foreign Body (IOFB), Fig. 1 Computed tomography of the brain and orbits demonstrates a metallic intraorbital foreign body located deep in the orbit. Axial (b), coronal (c) and sagittal (d) sections further delineate the proximity of the foreign body to the optic nerve

hemorrhage, chemosis, corneal abrasion, hyphema, iris sphincter tear, and iridodialysis. Importantly, a retrospective consecutive case series by Fulcher et al. (2002) showed that ruptured globe was the most commonly associated ocular injury. Fundoscopic examination may reveal traumatic posterior vitreous detachment and vitreous hemorrhage. With more serious compressive injury, retinal breaks, retinodialysis, choroidal rupture, or sclopetaria may develop.

Diagnostics

Computed tomography (CT) is the modality of choice as it provides excellent soft tissue and bony detail, can detect the majority of foreign bodies, and is safe in the presence of metal. Generally, 1.5–3 mm axial and coronal images are preferred. Wooden foreign bodies may be missed on CT or misdiagnosed as intraorbital air. Magnetic resonance imaging (MRI) is better at

detecting these types of foreign bodies but should be performed only after the presence of metal is ruled out. Ultrasonography may be useful as an adjunctive study should CT and MRI prove equivocal.

Differential Diagnosis

Orbital tumor, idiopathic orbital inflammation, orbital or preseptal cellulitis.

Prophylaxis

Protective eyewear.

Treatment

A general management algorithm is outlined in Fig. 1. As mentioned previously, it is most important to first complete a systemic evaluation to rule out potentially life-threatening injuries and to rule out an ophthalmic emergency such as a ruptured globe. Afterwards, the extent of any ocular, adnexal, orbital, and adjacent sinocranial injuries can be addressed (Finklestein et al. 1997). Consultation with neurosurgery or otolaryngology may be required.

Empiric broad-spectrum antibiotics, often with the guidance of an infectious diseases specialist, should be administered. If concomitant traumatic optic neuropathy is present, the use of systemic corticosteroids remains controversial (Yu-Wai-Man and Griffiths 2007). There is currently insufficient evidence that systemic corticosteroids provide benefit in these cases. Appropriate imaging, as outlined above, can then be obtained to identify the foreign body.

Composition and location of the foreign body determine further management. Because of the increased risk for infection and inflammation, all organic foreign bodies should be removed, although there is a paucity of data on those located in the posterior orbit (Ho et al. 2004). The approach to inorganic foreign bodies is more complex. Those that are freely palpable and located in the anterior orbit should be removed. Those that are nonpalpable, biologically inert, and located in the anterior, epibulbar, or posterior orbit can usually be managed conservatively given the risk of hemorrhage and iatrogenic functional deficit during surgical extraction.

Although most metals are inert, there are three notable exceptions. Copper may induce a large degree of inflammation. Iron may cause localized siderosis and subsequent retinal degeneration detectable on electroretinogram (ERG). Lead may lead to systemic toxicity. Thus, for inorganic foreign bodies, removal should be considered in cases associated with severe inflammation, infection, functional deficit, or one of the above biologically intolerable metals.

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Intravitreal Injections

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Synonyms

Intraocular injection; Intravitreous injection

Definition

An intravitreal injection is the process in which a substance is directly deposited into the vitreous cavity by inserting a needle through the pars plana. The needle is attached to a syringe containing an agent that is then released into the vitreous cavity.

Several agents can be administered with intravitreal injections. Examples include:

- Antibiotics
- Gases (C3F8, SF6)
- Clot disrupting agents (recombinant tissue plasminogen activator, rTPA)
- Immunosuppressants (methotrexate, steroids)
- Enzymes (ocriplasmin)
- Antibodies, antigen-binding fragments, and soluble receptors

Inhibitors of vascular endothelial growth factor (VEGF) are the most common agents injected into the vitreous worldwide. These agents include Avastin (bevacizumab), Lucentis (ranibizumab), and Eylea (aflibercept) and are used for the treatment of exudative eye diseases such neovascular age-related macular degeneration, diabetic macular edema, and retinal edema associated with venous occlusions.

Procedure Technique

In order to minimize complications from intravitreal injections, proper sterile technique should be utilized. Below are the summarized steps to performing an intravitreal injection:

1. Informed consent and appropriate eye identified and marked for injection.
2. Instill the following series of drops several times:
   - One (1) drop of proparacaine
   - One (1) drop of lidocaine (4%)
   - One (1) drop of ophthalmic povidone–iodine (Betadine) (5%)
3. A Betadine swap to clean the eyelashes and eyelids is recommended. Clean from the inner canthus to the outer canthus, and then clean off the Betadine from the eyelids and eyelashes with a sterile eye pad.
4. Place an eyelid speculum in the eye.
5. Perform the following series of steps several times to lower the intraocular pressure and anesthetize the injection site:
   - Apply a cotton tip applicator soaked with 4% lidocaine approximately 3.5–4 mm posterior to the limbus in the superior of inferior temporal quadrants for a duration of 20–30 s. Most injectors prefer the inferior quadrant.
   - Apply the cotton tip applicator with firm pressure in the quadrant where the injection will be performed.
   - Lubricate the cornea surface with artificial tears.
6. Instill one (1) drop of 5% Betadine into the eye. To minimize the postinjection discomfort from 5% Betadine, pretreatment with topical ketorolac is recommended.
7. Use a sterile caliper to measure the site of injection (optional).
8. Instill one (1) drop of Betadine into the eye.
9. Prepare the medication in the appropriate syringe and needle (typically a 1 cc syringe with a 30- or 32-gauge needle, and needle length should be around ½ or 5/8 in.).
10. Prior to inserting the needle, everyone (physician, assistant, and patient) should refrain from speaking or should wear surgical masks to reduce the risk of infection.
11. Using a one-handed technique with a cotton tip swab in the fellow hand, the injector inserts the needle at the marked injection site, perpendicular to the sclera, and through the pars plana (typically 3.5 mm posterior to the limbus in pseudophakic eyes and 4 mm posterior to the limbus in phakic eyes). The needle should be directed toward the center of the vitreous cavity and buried until its hub touches the eye. The medication is then injected.
12. The needle is removed and the cotton tip swab is placed over the injection site.
13. Check for counting fingers or hand motion vision after the injection. If light perception

is not detectable within 5 min, then an anterior segment paracentesis is performed. A check of the intraocular pressure (IOP) within 5 min of the injection is optional, but recommended especially if vision is impaired.

Complications

The complications associated with intravitreal injections are few and are usually attributed to the injection technique, the volume injected, or the agent injected. The actual insertion of the needle is associated with complications that include damage to the natural crystalline lens, lens zonules, lens capsule, and retina, such as a retinal tear or detachment, which is related to the direction of the needle as it enters the eye. The volume injected into the eye is associated with an elevated intraocular pressure, which is usually transient, but if it persists, a paracentesis is needed or permanent damage to the vision could result. A recent study by Gregori et al. (2014) showed that decompressing the eye with a cotton tip applicator prior to the injection during the anesthetic step produced a significantly lower IOP spike postinjection.

Endophthalmitis can result from bacterial contamination from the surface of the eye, due to inadequate preparation of the eye, or from the needle if it becomes inadvertently contaminated. In addition, the agent injected into the eye could be contaminated during the preparation process, whether it is performed in the clinic or operating room when the drug is withdrawn from the vial or when the drug is prepared in the compounding pharmacy. Infectious endophthalmitis is rare, but is an emergency situation when it occurs and needs to be treated promptly with a vitreous tap and injection of antibiotics. Symptoms usually do not develop for several days depending on the type of bacteria and the bacterial load at the time of injection. Typical complaints include ocular pain, decreased vision, and a red, swollen eye. However, not all of these symptoms need to be present. It is crucial to differentiate an infectious endophthalmitis from a noninfectious or "sterile endophthalmitis," and this distinction may be challenging due to the overlap of signs and symptoms. In a sterile endophthalmitis, the eye is usually not as red and is less painful. It is also very rare to see fibrin or a hypopyon. The treatment for sterile endophthalmitis is usually topical steroids, and the condition may take several weeks to fully resolve.

Milder complications of intravitreal injections are small conjunctival hemorrhages that occur from the injection and transient ocular irritation, which can result in a "burning" sensation described by some patients after the injection. These conditions are self-limited and usually resolve within several days. Artificial tears are often helpful after an injection to help alleviate the irritation.

In the setting of a periocular infection such as an active chalazion, canaliculitis, or a severe case of blepharitis, it is advisable to postpone the injection until the infection has resolved. However, in certain patient situations, there are some exceptions when the benefits of the injection outweigh the potential risk of endophthalmitis, and this decision must be determined by the injecting physician (Avery et al. 2014).

Postinjection Antibiotics

No effect has been proven in lowering the risk of an intraocular infection with the use of topical antibiotics after intravitreal injections, and there is insufficient evidence to support the routine use of antibiotics to prevent endophthalmitis (Avery et al. 2014).

Cross-References

- ▶ Aflibercept
- ▶ Bevacizumab
- ▶ Ranibizumab

References

Avery RL, Bakri SJ, Blumenkranz MS (2014) Intravitreal injection technique and monitoring: updated guidelines of an expert panel. Retina 34(Suppl 12):S1–S18

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Intravitreal Triamcinolone

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Synonyms

The current commercial preparations of triamcinolone acetonide include Aristocort acetonide; Flutex; Kenacort-A; Kenalog; Kenaquart; Ledercort D; Oncilon-A; Respicort; Rineton; Solodelf; Tramacin; Tricinolon; Vetalog; Volonimat.

Definition

Injection of triamcinolone acetonide into vitreous cavity through pars plana.

Indication

(i) Edematous retinal diseases including diffuse diabetic macular edema, macular edema secondary to branch retinal vein occlusion and central retinal vein occlusion, persistent pseudophakic cystoid macular edema, radiation-induced macular edema, cystoid macular edema due to retinitis pigmentosa, panretinal photocoagulation, adult Coat's syndrome, penetrating keratoplasty, and Behcet disease

(ii) Neovascular retinal or choroidal diseases including proliferative diabetic retinopathy, and diabetic retinopathy in general, exudative age-related macular degeneration, myopic choroidal neovascularization, choroidal neovascularization in Sorsby's fundus dystrophy, and neovascular glaucoma without or with cataract surgery

(iii) Intraocular inflammation including chronic uveitis, presumed ocular histoplasmosis syndrome, sympathetic ophthalmia, immunologic corneal graft reaction, Vogt-Koyanagi-Harada syndrome, and chronic prephthisical ocular hypotony

(iv) Others including perifoveal telangiectasia, ischemic ophthalmopathy, extensive exudative retinal detachment, and prevention of proliferative vitreoretinopathy, and in combination with intraocular surgery to visualize the vitreous

Contraindication

(i) Infective endophthalmitis
(ii) History of steroid-induced glaucoma
(iii) Viral retinal diseases including acute retinal necrosis and cytomegalovirus retinitis

Use and Dosage

Intravitreal injection of triamcinolone acetonide with dosage varied from 1.0 to 20.0 mg. In most cases, it is 4.0 mg. In nonvitrectomized patient eyes, the mean elimination half-life was 18.6 days, while in one postvitrectomy patient eye, it decreased to 3.2 days. After single intravitreal injection, peak aqueous humor concentrations ranged from 2.15 to 7.20 μg/ml. Electroretinogram and histologic sections in silicone-filled rabbit eyes after intravitreal injection of triamcinolone acetonide with dosage of 1 mg, 2 mg, or 4 mg were normal (Kivilcim et al. 2000).

Adverse Reactions

(i) Postinjection infectious endophthalmitis: The frequency of postinjection infectious endophthalmitis as reported ranged between 0/700 and 8/992 (0.87%) (Jonas et al. 2005). The risk of an infectious endophthalmitis may partially depend on the setting of the injection itself. Histologically, eyes with intravitreal triamcinolone acetonide and infectious endophthalmitis show a marked destruction of the whole globe. The most striking finding can be that some areas show a massive infiltration by granulocytes, while other areas can be almost completely devoid of inflammatory cells.

(ii) Postinjection pseudo-endophthalmitis: Triamcinolone acetonide crystals can mimic a so-called pseudo-hypopyon, if they penetrate from the vitreous cavity into the anterior chamber. The diagnostic problem is the differentiation between a painless hypopyon caused by a postinjection infectious endophthalmitis and a pseudo-hypopyon due to triamcinolone acetonide crystals. Using high magnification slit lamp biomicroscopy usually reveals the crystalline structure of triamcinolone acetonide.

(iii) Secondary ocular hypertension, secondary steroid-induced open-angle glaucoma: Studies have noted the prevalence of intraocular pressure elevations after intravitreal injection of triamcinolone to vary between 28% and 77%. Young people are mainly involved. The rise in intraocular pressure started at about 1 week after the injection, and the measurements returned to the baseline values after about 9 months. A prospective clinical interventional comparative nonrandomized study included 260 consecutive patients (293 eyes) receiving an intravitreal injection of 20–25 mg triamcinolone acetonide as treatment for diffuse diabetic macular edema, exudative age-related macular degeneration, retinal vein occlusions, uveitis, and cystoid macular edema. Intraocular pressure readings higher than 21 mmHg, 30 mmHg, 35 mmHg, and 40 mmHg, respectively, were measured in 94 (36.2%) patients, 22 (8.5%) patients, 11 (4.2%) patients, and 4 (1.5%) patients, respectively. Triamcinolone-induced elevation of intraocular pressure could be treated by antiglaucomatous medication in all but 3 (1.0%) eyes, for which filtering surgery became necessary (Tao and Jonas 2011). However, postinjection rise in intraocular pressure did not vary significantly between patients with a preinjection diagnosis of chronic open-angle glaucoma and patients without history of glaucoma.

(iv) Rhegmatogenous retinal detachment: Rhegmatogenous retinal detachment is a theoretical risk and rare case report can be found in pervious literature.

(v) Postinjection, steroid-induced cataract: Single intravitreal triamcinolone injection induced posterior subcapsular cataract development, whereas multiple injections resulted in all-layer cataract progression. Thompson studied by linear regression analysis lens scores from lens opacity standards in evaluating 93 eyes with intravitreal injection of 4 mg of triamcinolone acetonide. Lens opacities were graded using the Lens Opacity Classification System II (LOCS II) scale. This scale assigns a number between 0 and 4 for all lens opacities for three cataract types: nuclear sclerosis, posterior subcapsular cataracts, and cortical cataracts. Fractional scores were used if a cataract was between two standards, such as 0.5 for a cataract between the "0" and "1" standards. Nuclear sclerosis increased at a rate of 0.175 U per year, posterior subcapsular cataracts at 0.423 U per year, and cortical cataracts at 0.045 U per year (Thompson 2006).

(vi) Central serous chorioretinopathy: In a previous case report, a patient who developed central serous chorioretinopathy after vitrectomy with intravitreal triamcinolone acetonide for diabetic macular edema was reported (Imasawa et al. 2005).

(vii) Toxic effects: The intraocular use of Kenalog has not been proved by FDA. The preservative in Kenalog-40 is 0.99% benzyl alcohol, which may be potentially toxic to retina and lens, and it was supported by various animal studies from different groups of authors. Direct toxic effects of triamcinolone acetonide on the retina and optic nerve have not been observed yet, independently of the dosage used.

Interactions

Intravitreal triamcinolone has been reported to be safely used to be combined with some other drugs which are generally intravitreally used, such as ranibizumab and bevacizumab. Intravitreally injected triamcinolone acetonide does not mix with silicone oil. Triamcinolone acetonide crystals that sediment at the lower border of a silicone oil bubble may be harmful to retinal cells.

Cross-References

- ▶ Age-Related Macular Degeneration
- ▶ Central Retinal Vein, Occlusion of
- ▶ Corticosteroids
- ▶ Diabetic Macular Edema
- ▶ Macular Edema

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Intravitreous Injection

▶ Intravitreal Injections

Inversely Proportional to Wavelength

▶ Frequency of Light Wave

I

Inverted Follicular Keratosis

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Synonyms

Basosquamous cell acanthoma

Definition

Inverted follicular keratosis (IFK) is a benign usually solitary epithelial tumor that appears predominantly on the skin of the face.

Etiology

Histological studies from the past considered these lesions to be derived from a pilosebaceous unit. Therefore, IFK is an older term, but it is now

believed to represent a type of irritated seborrheic keratosis (Albert and Jakobiec 2008; Shields and Shields 2008).

Clinical Presentation

IFK presents clinically as a circumscribed keratotic growth located on or near the eyelid margin. It may grow up in many patterns: nodular, papillomatous, verrucous (wartlike), cystic, or rarely as a cutaneous horn or is pigmented. After trauma, the epithelium of the lesion may become scab and lead to burning, itching, or bleeding. It occurs most often in white males, middle-aged or older, and may develop rapidly over months.

Diagnostics

Clinical appearance and/or histopathology.

Differential Diagnosis

Differential diagnosis includes ▶ melanoma, ▶ melanocytic nevus ▶ pigmented basal cell carcinoma ▶ cutaneous horn, ▶ verruca vulgaris, and granuloma.

Prophylaxis

Uncertain.

Therapy

Observation, but excision, when the lesion is small, is reasonable for cosmetic reasons.

Prognosis

Excellent prognosis. Recurrence is infrequent after adequate excision.

Epidemiology

Uncertain.

Cross-References

- ▶ Basal Cell Carcinoma of Eyelid
- ▶ Choroidal and/or Ciliary Body and/or Iris Melanoma
- ▶ Cutaneous Horn
- ▶ Verruca Vulgaris

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Albert D, Jakobiec F (2008) Principles and practice of ophthalmology, 3rd edn. Saunders, Philadelphia, pp 3249–3250

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IOL

▶ Intraocular Lens

IOL Haptic

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Definition

The part of an ▶ intraocular lens (IOL) that connects the optic of the IOL with the intraocular tissue and thus maintains the desired IOL position.

Basic Characteristics

While Harold Ridley's first IOL from 1949 consisted of just an optical part, modern IOLs consist of an optic (the "lens" itself) and a haptic part that connects the optic to the surrounding

tissue. The haptic design depends from the desired location of the IOL within the eye. The first IOLs with haptics were anterior chamber IOLs with haptics designed to fit in the angle. Correspondingly, there were/are haptic types designed for fit in the pupil (Fyodoroff and Binkhorst), the iris (e.g., ▶ Artisan™/Verisyse™), the ciliary sulcus (e.g., Sulcoflex™, Visian™, and many others), and most importantly the capsular bag. IOLs for the capsular bag and the ciliary sulcus are typically equipped with loop- or plate-shaped haptics, while anterior chamber IOLs have Z-shaped haptics providing high rotational stability. Iris-fixated IOLs need claw haptics that grab a small fold of iris tissue. In single-piece IOLs, the material of the haptics is identical to the material of the IOL optic. Three-piece IOLs have haptics made from a material different from the optic (e.g., polypropylene or PMMA). So-called ▶ "accommodative" IOLs have haptics designed to transmit the action of the ciliary muscle to the IOL optic.

Cross-References

- ▶ Accommodating Intraocular Lens
- ▶ Artisan Lens
- ▶ Intraocular Lens

IOP

- ▶ Intraocular Pressure

Iridocorneal Endothelial (ICE) Syndrome

- ▶ Chandler Syndrome

Iridocorneal Endothelial Syndrome (ICE)

- ▶ Corneal Dystrophies

Iridocorneo Endothelial Syndrome

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Synonyms

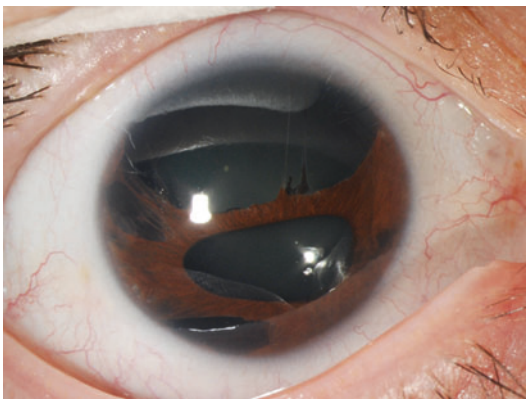
Chandler syndrome; Cogan-Reese syndrome; ICE syndrome; Iris nevus syndrome; Progressive iris atrophy; Proliferative endotheliopathy

Definition

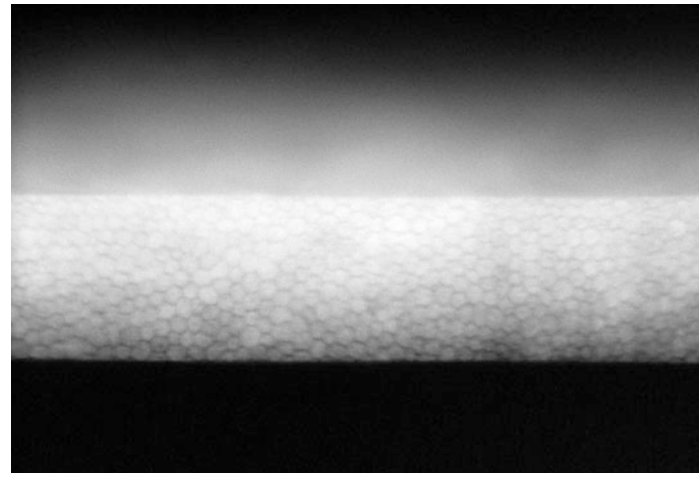
ICE syndrome is typically an unilateral condition with three clinical variants:

- (Fig. 1)
- Iris nevus syndrome (Cogan-Reese syndrome)
- Chandler syndrome

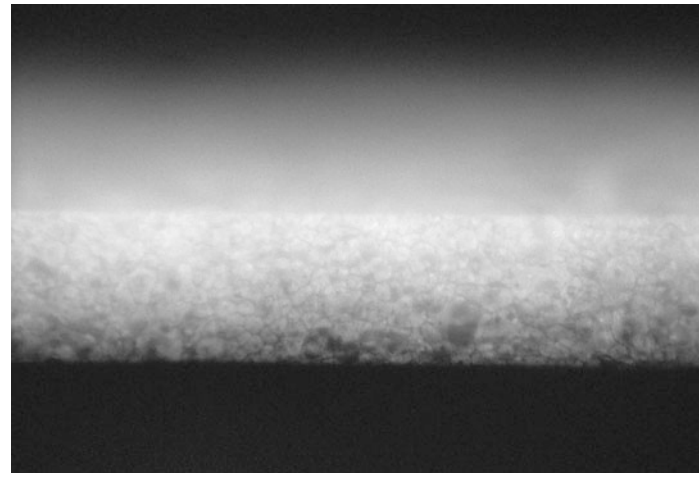
All three entities might be overlapping but have in common an abnormal corneal endothelium (Fig. 2 normal and Fig. 3 abnormal endothelium) that proliferates and migrates across the trabecular meshwork onto the surface of the iris.



Iridocorneo Endothelial Syndrome, Fig. 1 Presenting with progressive irisatrophy in ICE syndrome

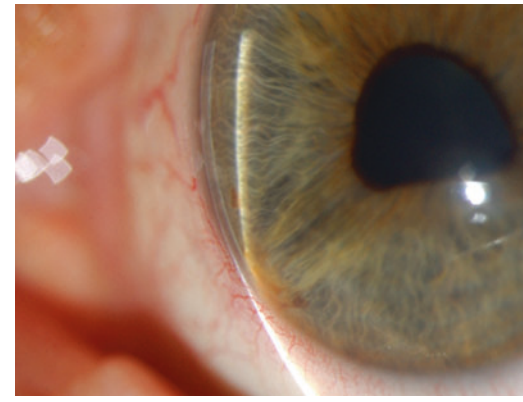


Iridocorneo Endothelial Syndrome, Fig. 2 Norman coneal endothelium with regular size and number of endothelial cells



Iridocorneo Endothelial Syndrome, Fig. 3 In ICE syndrome, corneal endothelial cells are abnormal in number, shape, and size

Contraction of abnormal endothelial tissue on the surface of the trabecular meshwork and iris root leads to anterior synechias (PAS) (Figs. 4 and 5), obstruction of the aqueous outflow and, finally, to secondary angle-closure glaucoma (Fig. 6: UBM of closed angle). Corneal endothelium insufficiency with decompensated corneal edema may be seen with or without glaucoma.



Iridocorneo Endothelial Syndrome, Fig. 4 Anterior synechias are often present

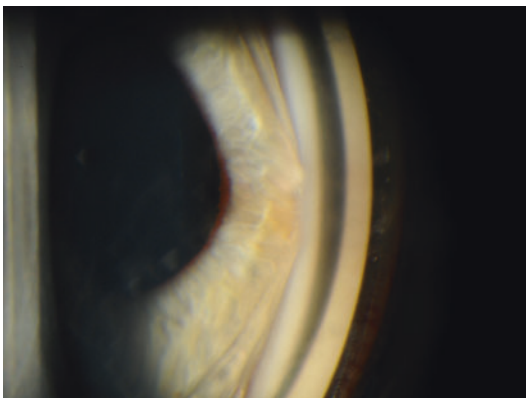
Etiology

Etiology is unknown. However, in some cases of ICE syndrome Epstein-Barr or herpes simplex

viruses are seropositive or might be found by polymerase chain reaction (PCR) in corneal probes. An underlying viral infectious disease is discussed.

Clinical Presentation

ICE syndrome is asymptomatic in its early stages. Later on, iris abnormalities, blurred vision caused by corneal edema, or pain could be found. ICE syndrome typical occurs in young to middle-aged adults (between 20 and 50 years of age). The disease is seen more often in females than in males. A family predisposition is extremely rare.



Iridocorneo Endothelial Syndrome, Fig. 5 Anterior synechias occluding parts of trabecular meshwork

No association with other ocular or systemic disease has been found.

Severe iris atrophy and heterochromia is characteristic for progressive iris atrophy. Also corectopia, ectropion uveae, iris stromal and pigment epithelial atrophy, and iris holes may be found. In Chandler syndrome, the corneal and angle findings are predominant with only minimal iris atrophy. Chandler syndrome is the most common entity with up to 50% of all ICE syndromes. Cogan-Reese syndrome represents with less iris atrophy but nodules or diffuse pigmented lesions on the anterior iris surface.

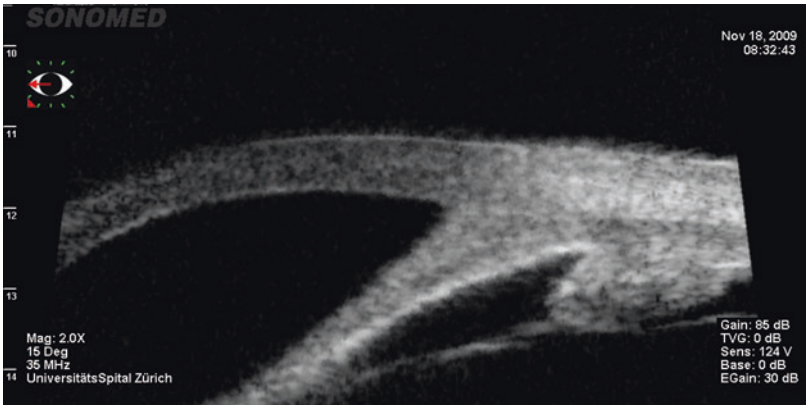
Glaucoma occurs in 50% of all ICE syndrome cases. The glaucoma seems to be more severe in Cogan-Reese syndrome and progressive iris atrophy than in Chandler syndrome. The three entities may overlap.

Diagnosis

Always consider ICE syndrome in cases of chronic and progressive unilateral pressure raise of young to middle-aged patients.

Specular microscopy is able to identify unilateral loss of endothelial cells and migration of endothelium on the trabecular meshwork or on the iris surface. Also consider endothelium cell count to identify an asymmetric cell loss in one eye (Hirst LW et al. 1980).

Iridocorneo Endothelial Syndrome, Fig. 6 Ultrasound biomicroscopy (UBM) reveals angle obstruction (secondary angle-closure)



Differential Diagnosis

- Fuchs' endothelial dystrophy (usually bilateral)
- Iris melanoma
- Axenfeld-Rieger syndrome (Dysgenetic chamber angle)
- Chronic uveitis (associated with endothelial precipitates)
- Posterior polymorphous dystrophy (usually bilateral)

Therapy

Treatment should be initialized when glaucoma or cornea edema occurs. The glaucoma associated with ICE syndrome is often difficult to treat. Possible therapeutical procedures include:

1. Antiglaucomatous medication (laser trabeculoplasty is ineffective)
2. Hypertonic salt solution to reduce corneal edema (e.g., 5% sodium chloride solution)
3. Corneal transplantation
4. Filtering surgery (tube shunts have a better survival rate compared to trabeculectomies (Stamper et al. 2009)) (Doe EA et al. 2001)

Prognosis

Secondary glaucoma in ICE syndromes is often difficult to treat and shows a poorer prognosis compared to other types of open angle and angle-closure glaucoma.

Epidemiology

The rate of glaucoma associated with ICE syndrome ranges between 46% and 82%.

Cross-References

- ▶ Chandler Syndrome
- ▶ Cogan Syndrome
- ▶ Fuchs Dystrophy
- ▶ Fuchs Heterochromic Iridocyclitis, Glaucoma
- ▶ Heterochromic Cyclitis Fuchs' Glaucoma
- ▶ Progressive Iris Atrophy

References

Doe EA, Budenz DL, Gedde SJ, Imami NR (2001) Long-term surgical outcomes of patients with glaucoma secondary to the iridocorneal endothelial syndrome. Ophthalmology 108:1789–1795

Hirst LW, Quigley HA, Stark WJ, Shields MB (1980) Specular microscopy of iridocorneal endothelial syndrome. Am J Ophthalmol 89:11–21

Stamper RL, Lieberman MF, Drake MV (2009) Becker-Shaffer's diagnosis and therapy of the glaucomas. Mosby Elsevier, London

Iridotomy

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Synonyms

Laser iridotomy

Definition

Surgical procedure in which a laser is used to create an artificial hole in the iris periphery. This opening in the iris equalizes the pressure between the front and the back of the iris and is mostly used for treatment of acute angle closure glaucoma.

Epidemiology

Due to the fact that acute angle closure glaucoma occurs in one of 1000 individuals, the incidence of iridotomies has similar numbers. Angle block glaucoma usually appears in individuals with narrow

angle. Most of the laser iridotomies are performed in individuals with 40 years of age or older.

History

The first iridotomies were performed in the late 1960s when ophthalmic laser systems were introduced. Argon laser iridotomies are being done since 1990.

Clinical Features

Selection of the correct laser is crucial for the outcome of the iridotomy. The Nd-YAG laser is used by most of the surgeons. This laser usually emits light with a wavelength of 1064 nm and operates in either pulsed or continuous mode. Usually 1–10 laser bursts with an energy of 4–6 mJ each are used for an iridotomy.

Tests

Slit lamp examination of the eye has to be performed prior to iridotomy. A hazy cornea is a contraindication for iridotomy. Patients also must receive miotic (usually pilocarpine) eye drops as well as topical anesthesia. Finally, an iridotomy treatment contact lens must be used.

Differential Diagnosis

Other intraocular pressure sinking methods are as follows:

- Iridectomy
- Trabeculectomy
- Sclerotomy
- Drainage implants

Etiology

Angle closure is a result of obstruction of the trabecular meshwork by the peripheral iris. This can be due to a narrow anterior chamber angle, a pupillary block mostly in hyperopic patients or mydriasis.

Treatment

After the patient has been brought in the correct position and has received topical anesthesia, an iridotomy lens is placed on the cornea using a coupling agent such as methylcellulose. Then, the surgeon has to localize an iris crypt, usually between 11 and 1 o'clock position, and focus the laser beam slightly anterior to the focus of the aiming beam. When focused properly, the laser energy is applied to the iris. The process is successful when the iris epithelium is perforated and a gush of fluid flows through the iridotomy from the posterior chamber into the anterior chamber.

Cross-References

▶ Angle-Closure Glaucoma

Further Reading

Albert DM, Miller JW, Azar DT (2008) Albert & Jakobiec's principles & practice of ophthalmology. Saunders, Philadelphia

Schacknow PN, Samples JR (2010) The Glaucoma book: a practical, evidence-based approach to patient care. Springer, Berlin

Iris Coloboma

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Synonyms

Iris defect; Keyhole pupil

Definition

The term coloboma is derived from the Greek word *koloboma* and means a mutilated or curtailed structure. Accordingly an iris coloboma is a notch, gap, hole, or fissure in the iris of varying depth, giving the pupil an irregular shape. Iris coloboma can be due to congenital or traumatic causes (injury/surgical) and can appear complete or incomplete and typical or atypical and may extend to lens, ciliary body, zonula fibers, retina, choroid, or optic nerve. Main symptoms of an iris coloboma can be blurred vision and glare followed by decreased vision acuity.

Histology

Colobomata generally result from a failure of the fetal or choroidal fissure to close during the fifth to seventh week of fetal life, at the 7–14 mm stage. This is the period between the invagination of the optic vesicle and the closure of the fetal fissure. A complete iris coloboma is a full-thickness defect, involving both the pigment epithelium and the iris stroma. An incomplete iris coloboma is usually partial thickness, involving either the pigment epithelium or the iris stroma. The "typical" coloboma is in the inferonasal quadrant, caused by defective closure of the fetal fissure. Iris coloboma located anywhere other than the inferonasal quadrant is termed "atypical." The embryologic basis of this malformation is still unclear, although several theories have been suggested.

Immunohistochemistry

There are no data available in this topic.

Electron Microscopy

There are no data available in this topic.

Molecular Diagnostics

The incidence of isolated iris coloboma is 1:6000. Commonly inheritance is autosomal dominant, but in some singular cases, autosomal recessive heredities or spontaneous mutations have been described.

Differential Diagnosis

A lot of syndromes are associated with iris coloboma such as:

- Autosomal-dominant uveal coloboma
- Cat-eye syndrome
- Edwards' syndrome
- Patau's syndrome
- Linear nevus sebaceous syndrome

Cross-References

▶ Ciliary Body
▶ Optic Nerve (Cranial Nerve II)

References

Burow B, Thiele U (1973) Genetic advice in ocular diseases. Albrecht Von Graefes Arch Klin Exp Ophthalmol 188:307–321

Onwochei B (2000) Ocular colobomata. Surv Ophthalmol 45(3):175

Iris Defect

▶ Iris Coloboma

Iris Deficiency

▶ Traumatic Aniridia

Iris Hooks

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Synonyms

Iris retractor

Definition

Iris hooks are small surgical devices that are used in anterior chamber operations for grasping, manipulating, stretching, retracting, or stabilizing the iris. These instruments are long, thin titanium slats with an arcuate end. Their domains are complicated surgical cases with narrow pupils or the intraoperative management of complications of the iris, e.g., iris prolapse or lens-iris diaphragm retropulsion syndrome.

Epidemiology

Iris hooks are not commonly used in ophthalmic surgery. The decision whether to use iris hooks, which require insertion through additional limbal incisions, or to choose another strategy is dependent on surgical skill, preference, and the operative situation.

History

Pupils that do not dilate adequately medicamentally for cataract extraction must be dilated manual. In former times different types of surgical enlargement were described such as radial iridotomy, sector iridectomy, multiple sphincterotomies, and/or iris retraction with a spatula or a suture. In 1990 Fuller et al. announced new instruments for pupil retraction with the aim of reducing or eliminating the need to incise or suture it. This instrument was the translimbal iris retractor, progenitor of the modern iris hook. In 1992 Mackool et al. designed iris retractors that have small hooks connected to small blocks of titanium that can be used without assistance to retract the iris. In 1997 flexible iris hooks made from modified material and in 1999 a double-hook iris retractor were established with the aim to prevent the retractor from dropping out of corneal incision, especially in anterior vitrectomy. In 2009 Böhm et al. described a new, modern irrigating iris retractor for cataract surgery in eyes with small pupils. This device consists of about two standard side-port irrigating openings and a smooth, button-like iris hook in the front designed for bimanual cataract extraction in cases with small pupils.

Clinical Features

A small pupil presents a challenge for cataract surgeons. It is commonly seen in eyes with pseudoexfoliation syndrome, secondary to anterior uveitis with central posterior synechiae; in patients with advanced age, diabetes, or glaucoma with miotic therapy, after trauma or previous surgery; and in the intraoperative floppy iris syndrome (IFIS). Until today there is no general solution for the problems that small pupils bring to cataract surgery.

Etiology/Treatment

See "Clinical Features" section above.

Cross-References

► Anterior Vitrectomy
► Iridotomy
► Iris Prolapse

Further Reading

Böhm P et al (2009) Irrigating iris retractor for complicated cataract surgery. J Cataract Refract Surg 35: 419–421
Mackool R (1992) Small pupil enlargement during cataract extraction; a new method. J Cataract Refract Surg 18:523–526
Novak J (1997) Flexible iris hooks for phacoemulsification. J Cataract Refract Surg 23:828–831

Iris Nevus Syndrome

► Iridocorneo Endothelial Syndrome

Iris Prolapse

► Traumatic Aniridia

Iris Prosthesis

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Synonyms

Artificial iris implant; Iris prosthetic implants; Iris reconstructive implant

Definition

Implantable ophthalmic devices for the management of partial or total aniridia. Iris prosthesis devices are developed for the reconstitution of a deformed or imperfectly functioning iris. There are different existing types of iris prosthesis devices made from variable materials. Their domain depends on the degree and severity of the iris defect.

Epidemiology

There exist no data in this topic.

History

In 1956 Peter Choyce developed the first iris prosthetic implant, an anterior lens, in the UK. In the 1970s John Pearce implanted a matutional iris diaphragm. The first reported implantation of the black iris diaphragm intraocular lens was in 1994 by Reinhard and Sandmacher et al. In 1996 Rosenthal K. reported the small-incision technique of iris prosthetic implants. In 2004 Rosenthal K. and Rasch V. invented a series of aniridia and coloboma aperture rings to be implanted in an intact capsular bag, with or without zonular instability and with a separately implanted IOL.

Clinical Features

Iris defects occur in a variety of conditions, including congenital aniridia, coloboma, iridocorneal endothelial syndrome, Axenfeld-Rieger syndrome, trauma (surgical and non-surgical), uveitis, and idiopathic postoperative mydriasis. With iris and lens abnormalities, these conditions lead to cosmetic and optical defects. An intact iris diaphragm is essential as it reduces the optical aberrations arising from the crystalline lens and thereby increases the depth of focus. Thus, total aniridia is known to cause incapacitating glare and photophobia.

Test

Success of an iris prosthesis implant can be tested with the best and uncorrected vision acuity in different illumination shades and detailed slit-lamp examination.

Etiology

See "Clinical Features" section above.

Treatment

For the treatment of partial or total aniridia, there exist several different iris prosthesis implants and their use is dependent on the severity of the iris defect. For cases with partial defects, endocapsular ring prosthetic devices exist with multiple- or single-fin style. Other possibilities for the correction of combined aniridia and aphakia are single-piece (black) iris diaphragm intraocular lenses. Iris diaphragm rings or iris prosthetics with different colors and designs are for used in cases with or without capsular bag or zonular support. Furthermore there are differences in the size of the incision. Small-incision techniques need 3–5 mm incision and other implants or techniques need 10–12 mm incisions.

Cross-References

► Aniridia, Traumatic

Further Reading

Burk SE et al (2001) Prosthetic iris implantation for congenital, traumatic, or functional iris deficiencies. J Cataract Refract Surg 27:1732–1740
Rosenthal K (2004) Iris prosthesis/IOL implantation. Cataract Refract Surg Today 78–80

Iris Prosthetic Implants

► Iris Prosthesis

Iris Reconstructive Implant

► Iris Prosthesis

Iris Retractor

► Iris Hooks

Iris Suture Fixation

► McCannel Technique

Iris, Characteristics

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Definition

The anterior, visible part of the uveal tract composed of two layers – the iris pigment epithelium and the iris stroma.

Basic Characteristics

The iris, named after the Greek goddess of the rainbow, is responsible for eye color. The iris pigment epithelium is derived from the neuroectoderm, and the iris stroma is derived from the neural crest. The stroma contains nonpigmented and pigmented cells in a matrix of collagen fibrils and glycosaminoglycans. In lighter irides, the anterior melanocytes lack pigment and are transparent. In darker irides, the melanocytes are opacified by pigment with an increased number and size of melanin granules.

The thickest portion of the iris is the collarette which separates the peripheral ciliary zone from the papillary zone; the pupillary portion of the iris is thinner due to embryological resorption of the pupillary membrane and formation of the papillary aperture.

The sphincter and dilator muscles of the iris control the amount of light which enters the eye. Short ciliary nerves arising from the ciliary ganglion and containing postganglionic parasympathetic fibers innervate the sphincter muscle; postganglionic sympathetic fibers from superior cervical sympathetic ganglion travel with the long ciliary nerves and innervate the dilator muscle.

The major arterial circle in the ciliary body near the iris root supplies blood to the iris through branches which travel radially toward the collarette where they form an incomplete minor arterial circle from which branches radiate toward the pupil to supply the sphincter muscle and radiate toward the iris root along with the dilator muscle. Histologically unique, iris vessels are cloaked by a thick layer of collagen fibers and are visible in lighter irides.

The iris is affected in many ocular and systemic diseases, and assessment of pupillary function allows one to evaluate normal and abnormal functioning of the afferent and efferent pathways.

Cross-References

- ▶ Adie's Pupil
- ▶ Afferent Pupillary Defects, Relative (Marcus Gunn Pupil)
- ▶ Aniridia, Traumatic
- ▶ Anisocoria
- ▶ Argyll Robertson Pupil
- ▶ Axenfeld-Rieger Syndrome; Mesodermal Dysgenesis; Leukomas
- ▶ Choroidal and/or Ciliary Body and/or Iris Melanoma
- ▶ Horner's Syndrome
- ▶ Iridocorneal Endothelial Syndrome (ICE)
- ▶ Iris Coloboma
- ▶ Iris Nevus Syndrome
- ▶ Persistent Pupillary Membrane
- ▶ Progressive Iris Atrophy
- ▶ Pupil Center
- ▶ Swinging-Light Test, for RAPD Identification

Further Reading

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Eagle RC (2011) Eye pathology: an atlas and text, 2nd edn. Lippincott, Williams & Wilkins, Philadelphia, pp 6–7

Iris-Fixated Phakic Intraocular Lens

- ▶ Artisan Lens
- ▶ Verisyse Iris-Supported Phakic Intraocular Lens

Iron Line

- ▶ Hudson-Stähli Line

Iron Lines

- ▶ Iron, Corneal Deposits of

Iron Lines, Pterygium

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Synonyms

Stocker line

Definition

Iron deposit in the corneal epithelium at the leading edge of a pterygium.

Etiology

Iron lines are often believed to form due to abnormal pooling of tear related to surface irregularities in long-standing pterygium (Loh et al. 2009).

Clinical Presentation

Pigmented line at the anterior edge of the pterygium, often best seen with red-free or cobalt blue illumination.

Diagnosis

Stocker line can be diagnosed based on the presence of pterygium and clinical examination.

Differential Diagnosis

Stoker line can be differentiated from other iron deposits in the cornea including Hudson-Stähli line seen in healthy aging cornea, Ferry line anterior to filtering bleb, Fleischer ring in keratoconus, and iron lines in keratorefractive procedures.

Prophylaxis

None

Therapy

None

Prognosis

Benign condition

Epidemiology

Unknown

Cross-References

► Iron, Corneal Deposits of
► Pterygium

References

Loh A, Hadziahmetovic M, Dunaief JL (2009) Iron homeostasis and eye disease. Biochim Biophys Acta 1790(7):637–649

Iron Overload

► Hemochromatosis

Iron, Corneal Deposits of

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Synonyms

Ferry line; Fleischer ring; Hudson-Stähli line; Iron lines; Stocker line

Definition

Iron deposit in the corneal epithelium

Etiology

Iron lines are often believed to form due to abnormal pooling of tear related to surface irregularities. But alternative hypotheses including basal-cell-migration theory, tear desiccation hypothesis, senescent basal-cell hypothesis, and lactoferrin/transferrin receptor hypothesis exist (Loh et al. 2009).

Occurrence

The Hudson-Stähli line is formed at the lower third of otherwise healthy corneas and its occurrence increases with age. Fleischer ring is pigmented circumferential line at the base of the cornea in keratoconus. Ferry line is formed anterior to a filtering bleb. Stocker line is iron deposit

at the leading edge of a pterygium. Iron lines have also been associated with corneal trauma, Salzmann's nodular degeneration, and keratorefractive procedures.

Classification

Common iron lines are Hudson-Stähli line, Fleischer ring, Ferry line, and Stocker line.

Cross-References

- ▶ Iron Lines, Pterygium
- ▶ Keratoconus
- ▶ Pterygium

References

Loh A, Hadziahmetovic M, Dunaief JL (2009) Iron homeostasis and eye disease. Biochim Biophys Acta 1790(7):637–649

Iron, Corneal Intraocular Foreign Body of

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Synonyms

Rust ring; Siderosis

Definition

Iron is a magnetic metal that exists in a wide range of oxidation states, although +2 and +3 are most common. Fresh iron surfaces are silver-gray but oxidize in air to yield hydrated iron oxides, known as "rust." Iron oxides occupy more volume than iron metal. Iron plays an important role in the human body including forming complexes with oxygen to produce hemoglobin and myoglobin. It is also the active site of many important enzymes involved in oxidation and reduction reactions. Iron is a frequent cause of foreign bodies embedded within the cornea.

Etiology

Iron-containing foreign bodies (e.g., BB gun pellets, gunshot pellets, household items, nails, bolts, bridges, machinery, etc.) can embed themselves into the corneal substrate by numerous mechanisms. Frequently the edges of these foreign bodies are sharp enabling them to penetrate the cornea, and they may be quite hot as well, allowing them to melt their way into the cornea.

Clinical Presentation

Patients usually present with sudden eye pain, tearing, and redness, coinciding with a suggestive history such as doing metal-on-metal work or being in an environment conducive to flying metal particles. Blurred vision may be present.

Diagnosis

Physicians should obtain a thorough history, focusing on metal-on-metal work with the possibility of metal striking the eye at a high velocity. The metal can often be seen with direct illumination. Slit-lamp examination with fluorescein dye can further characterize the depth and extent of injury. Iron in its neutral form is relatively insoluble in the corneal layers. The metal's surface oxidizes and diffuses into the stroma, causing an immune cellular infiltrate. The combination of oxidized iron and cellular infiltrate clinically

correlate to a rust ring. These rust rings are usually seen at the level of the superficial stroma and can begin to form after just a few hours. Iron has a predilection for the corneal stroma and corneal endothelial cells. The wound site may be cultured if it appears infected. During exam, careful attention should be paid to assure that the metal is confined to the cornea and that there is no intraocular metallic penetration. Imaging modalities such as CT (1 mm sections through orbits) and ultrasound may aid in the diagnosis. MRI is contraindicated in the presence of a metallic foreign body such as iron.

Differential Diagnosis

Differential diagnosis includes non-iron-containing foreign bodies and other iron deposits such the Hudson-Stahli line (interpalpebral fissure), Fleischer ring (keratoconus), Stocker line (pterygium), and Ferry line (filtering blebs).

Prophylaxis

Avoidance of activities conducive to flying small pieces of metal or the use of protective eyewear if those activities are unavoidable.

Therapy

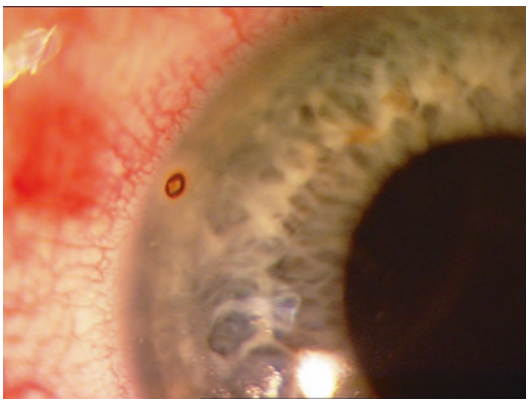
Corneal foreign bodies and rust rings can be removed at the slit lamp under topical anesthesia (e.g., proparacaine) with a cotton-tipped applicator, disposable small-gauge needle, and/or fine forceps. Multiple superficial foreign bodies may be more readily removed by irrigation. Battery-powered burrs with a sterile tip may also be used. The goal of these procedures is to remove the foreign body and rust ring with minimal tissue disruption to minimize complications and scar formation. Not all rust needs to be removed, particularly if removal results in scar tissue affecting the visual axis. It is often easier to remove the foreign body initially and the rust ring after several days. Treatment with topical antibiotics is wise after removal of these foreign bodies. If the clinical examination is suggestive of intraocular foreign body, appropriate surgical referral often with a retina specialist should be instituted immediately.

Prognosis

If left embedded in the cornea, iron-containing corneal foreign bodies may cause continued inflammation and delayed healing. When intraocular, iron may cause siderosis that may manifest as anisocoria, iris heterochromia, corneal endothelial and epithelial deposits, anterior subcapsular cataracts, lens dislocation, retinal degeneration, and optic atrophy.

Epidemiology

This is a common condition, but the exact incidence is unknown. In one prospective study on superficial corneal bodies, 92% of patients were male with a mean age of 35 years. 32.7% of patients had positive cultures. The most common microorganisms isolated were *Streptococcus* and *Staphylococcus* (Fig. 1).



Iron, Corneal Intraocular Foreign Body of, Fig. 1 Photo courtesy of Jeffry Judelson, MD

Cross-References

- ▶ Corneal Pigmentations
- ▶ Intraorbital Foreign Body (IOFB)
- ▶ Iron, Corneal Deposits of
- ▶ Iron Lines, Pterygium
- ▶ Siderosis: Signs and Symptoms

Further Reading

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Witherspoon SR, Hogan RN, Petroll WM, Mootha VV (2007) Slit-lamp, confocal, and light microscopic findings of corneal siderosis. Cornea 26(10):1270–1272

Zuckerman BD, Lieberman TW (1960) Corneal rust ring. Arch Ophthalmol 63:254–265

Ischemic Infarct of the Choroid

- ▶ Elschnig Spots

Isolated Trabeculodysgenesis

- ▶ Primary Congenital Glaucoma

J

Jefferson Syndrome

► Cavernous Sinus Syndrome

Junctional Nevus

► Nevus, Junctional

Junctional Scotoma

► Anterior Chiasmal Syndrome
► Wilbrand Knee

Juvenile Epithelial Dystrophy (Meesmann Dystrophy)

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Synonyms

Meesmann epithelial corneal dystrophy (MECD); Stocker-Holt

Definition

Bilateral corneal dystrophy involving corneal epithelium.

Etiology

MECD is a genetic disorder with an autosomal dominant pattern of inheritance. Mutations in the genes coding cornea-specific keratins, K3 (chromosome 12q13) and K12 (chromosome 17q12), have been linked to disease pathology. These two cytokeratins are mainly found in corneal epithelium, and mutations will lead to epithelial fragility that spares limbal cornea (expressing keratins 5 and 14).

Presentation

MECD presents with bilateral, symmetric intraepithelial cysts involving central visual axis and mid-periphery of the cornea that are visible only with slit lamp biomicroscopy (especially on retroillumination). Although cysts appear in the first decade of life, most patients remain asymptomatic until middle age. Symptoms are usually mild and include recurrent irritation and decrease in visual acuity.

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Diagnostics

In MECD, microcysts are present throughout the corneal epithelium. These cysts contain degenerated epithelial cells and cellular debris that are periodic acid-Schiff (PAS) positive. Other characteristic findings include presence of electron-dense filamentary and granular material, so-called peculiar substance, in the epithelial cells and vacuolated, homogenous substance in the epithelial cysts (most commonly) and epithelial cells. There is no change in Bowman's layer; however, nonspecific thickening of epithelial basement membrane is usually present.

Differential Diagnosis

Lisch epithelial corneal dystrophy, epithelial basement membrane dystrophy, Reis-Buckler's.

Prophylaxis

Unclear

Treatment

Symptoms are generally mild and topical lubrication will suffice in most cases. In more severe disease, bandage contact lens and superficial keratectomy can be beneficial.

Further Reading

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Juvenile Glaucoma

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Synonyms

Juvenile glaucoma is called sometimes presenile glaucoma.

Definition

Juvenile glaucoma is defined by a primary open-angle glaucoma appearing between the 10th and 35th year of life.

Etiology

The exact mechanism remains unknown, but a decreased aqueous outflow is observed. In most cases juvenile glaucoma is transmitted in an autosomal dominant fashion, involving the MYOC gene on chromosome 1q21-q31. At the moment more than 70 mutations in this gene are identified. More than one gene is likely to be involved.

Clinical Presentation

The disease is asymptomatic until an advanced visual field loss appears. Some patients have blurred vision and sensitivity to light related to very high intraocular pressure with corneal edema.

Diagnosis

In contrary to normal pressure glaucoma, juvenile glaucoma presents with an elevated IOP $\geq$21 mmHg. Severe intraocular pressure increases are quite often. The optic nerve demonstrates typical glaucomatous changes with diffuse or more rarely focal reduction of neuroretinal rim resulting in progressive glaucomatous visual field defects.

Nerve fiber layer demonstrates a typical diffuse defect. Gonioscopy is characterized by wide open anterior chamber angle. Typical signs of dysgenetic anterior chamber angle such as anterior insertion of the iris and poorly differentiated structures are observed in some cases.

Differential Diagnosis

Close angle, pseudoexfoliation, pigmentary, uveitic, posttraumatic glaucoma and glaucoma associated with intraocular hemorrhage, corticosteroid treatment, and increased episcleral venous pressure.

Therapy

The treatment is primarily medical with topical medications that reduce the aqueous humor production or facilitating its outflow. The inefficient reduction of the IOP often requires incisional surgical procedures used in adult-onset open-angle glaucoma with the addition of goniotomy, any trabecular bypass, or, if ineffective, a glaucoma drainage device.

Prognosis

Juvenile glaucoma with an insufficient treatment can lead to blindness. Usually glaucoma screening is performed after the 40th year of life; therefore, juvenile glaucoma develops undetected at severe stage of disease in most of the cases.

Epidemiology

Valid data are not available. Prevalence of juvenile glaucoma might be underestimated. Nevertheless, juvenile glaucoma represents a low percentage of all glaucoma diseases.

Cross-References

- ▶ Developmental Glaucoma
- ▶ Open-Angle Glaucomas
- ▶ Optic Neuropathy
- ▶ Primary Congenital Glaucoma
- ▶ Uveitic Glaucoma

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J

Juvenile Lentigo

▶ Lentigo Simplex (Simple Lentigines)

Juvenile Macular Degeneration

▶ Fundus Flavimaculatus (Stargardt Disease/ Juvenile Macular Degeneration)

Juvenile Macular Dystrophy

▶ Fundus Flavimaculatus (Stargardt Disease/ Juvenile Macular Degeneration)

K

Kaposi Sarcoma

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Definition

Kaposi sarcoma is a malignant spindle-cell tumor that most commonly affects the skin, but can also involve mucous membranes, internal organs, lymph nodes, and ocular structures (Brun and Jakobiec 1997).

Background

Hungarian dermatologist Moritz Kaposi first described "idiopathic multiple-pigment sarcomas" of the skin in 1872, later known as Kaposi sarcoma (Brun and Jakobiec 1997). There are four forms of the disease. The "classic form" is seen in elderly Eastern European or Mediterranean men of Jewish ancestry and follows a more benign, indolent course. The "endemic form" is more aggressive with increased visceral involvement and seen predominately in equatorial Africa. The two remaining forms of the disease are immunocompromised and HIV/AIDS related. The immunocompromised form is rare and can follow organ transplantation or immunosuppression. The AIDS-associated form is the most common presentation of Kaposi sarcoma in the USA. Further, Kaposi sarcoma is the most common malignancy of HIV/AIDS patients. Since the AIDS epidemic, there has been a rise in the incidence of Kaposi sarcoma with ocular involvement as well as multiple reports of conjunctival disease as the initial manifestation of HIV (Jeng et al. 2007; Verma et al. 2008).

Etiology/Pathophysiology

Though there are four differing forms of Kaposi sarcoma, all involve some degree of immune system dysregulation (Verma et al. 2008). There is a complex interaction between the immune system, the environment, and infections such as HIV and human herpesvirus 8 (HHV-8)/Kaposi-sarcoma-associated herpesvirus (KSHV) that contribute to the development of this disease. The result of these interactions is the proliferation of spindle cells around abnormal vascular spaces. The cell of origin is controversial; candidates include lymphatic, endothelial, smooth muscle, or neural cells. Patients may have single or multiple lesions. Examination of viral HHV-8 DNA from multiple tumor sites in one patient reveals that each tumor arises independently confirming that this is a multifocal disease, not metastatic. There is growing evidence linking HHV-8 and Kaposi sarcoma. HHV-8

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DNA has been isolated from all forms of this disease. One study found anti-HHV-8 antibodies present in 88% of the AIDS-associated Kaposi sarcoma patients, in 30% of the HIV-positive sarcoma-free patients, and only in 1–4% of a control HIV-negative group. There are very few ocular-specific Kaposi sarcoma studies exploring this relationship (Jeng et al. 2007; Biswas and Sudharshan 2008). The infection route of HHV-8 is unclear, though circumstantial evidence favors sexual transmission. Coinfection with HIV and HHV-8 is common, and it has been observed that these individuals tend to develop Kaposi sarcoma within 10 years of seroconversion. The pathogenesis of how the HHV-8 infection leads to the development of Kaposi sarcoma is under investigation. HHV-8 has been implicated in other diseases, such as lymphoma and Castleman, and is known to induce the deregulation of oncogenes and oncosuppressor genes. In conjunction with an already weakened immune surveillance system associated with HIV/AIDS, this can lead to cell proliferation.

Epidemiology

Classic Kaposi sarcoma is most common in Sicily in 50–70-year-olds with 30.1 cases per million in men and 7.7 cases per million in women. In Africa, endemic Kaposi sarcoma has a reported prevalence of 37.7 cases per 100,000 in men and 20.5 cases per 100,000 in women. In the USA, Kaposi sarcoma is the most frequent tumor in HIV/AIDS patients with a prevalence of 20–30%. There is a higher risk of Kaposi sarcoma if HIV was contracted though sexual transmission, likely attributed to the increased risk of contracting HHV-8. Homosexual HIV-positive men are 20 times more likely to develop Kaposi sarcoma than those who contracted HIV from blood transfusions (Brun and Jakobiec 1997). The incidence of Kaposi sarcoma is declining, presumably due to the immune reconstitution achieved with highly active antiretroviral therapy (HAART) (Verma et al. 2008). The International Collaboration on HIV and Cancer reported a decline from 15.2 cases per 1000 person-years in 1992–1996 to 4.9 cases per 1000 person-years in 1997–1999. In the 1980s, Kaposi sarcoma was the presenting manifestation of AIDS in 10–15% of HIV-positive homosexual men and in 1–2% of other risk-factor groups. The incidence of Kaposi sarcoma as the presenting manifestation of AIDS has decreased from 2.6 per 100 persons in the early 1990s to 0.75 per 100 person-years in 1997. Prior to the AIDS epidemic, ocular involvement was rare, with fewer than 30 case reports. Since 1982 there was a dramatic increase in ocular involvement. In AIDS patients with Kaposi sarcoma, up to 20% have some form of ocular involvement, with conjunctival lesions accounting for 5–10% (Jeng et al. 2007).

Clinical Presentation

Kaposi sarcoma most commonly presents on the skin. Initially the lesions are dark bluish purple, flat, and nonpalpable or plaque-like with a normal-appearing surface (Brun and Jakobiec 1997). As the disease progresses, the lesions become round or oval and more nodular and may reach up to 3 cm. Usually these lesions are asymptomatic. AIDS-associated Kaposi sarcoma is more aggressive than the classic form with earlier lymph node and visceral involvement. The extent of the cutaneous disease does not correlate to the degree of visceral involvement. Ocular disease has been reported to involve the eyelids; the bulbar, tarsal, and forniceal conjunctivas; the plica semilunaris; the caruncle; the lacrimal sac; and rarely the orbit and lacrimal gland (Jeng et al. 2007, Biswas and Sudharshan 2008). Conjunctival Kaposi sarcoma is most commonly seen in the inferior fornix, then the bulbar conjunctiva, followed by the superior fornix. These lesions are bright red, slightly elevated, and mobile, easily mistaken for subconjunctival hemorrhage. They may change shape over time. Eyelid lesions are similar to other skin lesions, bluish purple, flat, or raised resembling ecchymosis. They may eventually interfere with eyelid function, induce eyelid malposition, and infrequently lead to pain and vision loss (Verma et al. 2008).

Diagnostics

Once Kaposi sarcoma is suspected, a thorough examination of the patient's skin and lymph nodes should be performed as well as blood testing for HIV. Diagnosis is confirmed with an incisional biopsy. Histology reveals a complex arrangement of capillary channels and vascular spaces without endothelium or "slits" often surrounded by malignant spindle cells.

Staging

The standard TMN staging system does not work well with Kaposi sarcoma, so an alternate staging system has been developed to stratify patients into low- and high-risk groups based on immune status, extent of tumor involvement, and presence of systemic disease (Verma et al. 2008). Low-risk patients have tumors confined to the skin, lymph nodes, or oral palate (non-nodular); a CD4 count greater than 150/mm^3; no history of opportunistic infections; thrush; unexplained fevers; more than 10% voluntary weight loss; or diarrhea persisting over 2 weeks. If there is any tumor-associated edema or ulceration, extensive involvement of the oral mucosa, gastrointestinal, or lesions in other viscera, then those patients are considered high risk. Further, if the CD4 count is less than 150/mm^3 and if any of the previous systemic signs or other HIV-related illnesses such as lymphoma or neurologic disease is present, they are considered high risk.

Differential Diagnosis

Subconjunctival hemorrhage
Conjunctival inflammation
Melanosis
Malignant melanoma
Squamous cell carcinoma
Pyogenic granuloma
Lymphangioma
Cavernous hemangioma
Nodular scleritis
Lymphoma

Prophylaxis

Primary prevention of exposure to HIV and HHV-8 includes sexual abstinence, condom use, and avoidance of IV drug use. Secondary prevention of Kaposi sarcoma in HIV-positive patients relies on maintaining immunocompetence through HAART.

Treatment

The restoration of the immune system with HAART can induce the resolution of Kaposi sarcoma even without disease-specific therapy (Verma et al. 2008). However, there is no evidence that any therapy is curative or that a complete response necessarily translates to prolonged disease-free intervals. Therefore, the goal in treatment is palliation when the disease is disfiguring, painful, or impairing function. Most ocular and periorbital lesions follow an indolent course, thus palliative treatment is not always necessary. Indications for treatment include loss of normal eyelid function, discomfort, or cosmesis. The treatment depends on the size and location of the tumor. Treatment options include surgical excision, local radiation, cryotherapy, subconjunctival interferon alpha-2a, and systemic chemotherapy (bleomycin, doxorubicin, and vinblastine as single agents or in combination have been reported). However, local recurrence occurs frequently with any form of treatment.

Prognosis

Prognosis depends on the stage of the Kaposi sarcoma and the status of the patient's immune system. The degree of immune system impairment seems to be the most important factor in survival.

Cross-References

► Vascular Tumors Disease of the Conjunctiva

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Kayser-Fleischer Ring

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Definition

Kayser-Fleischer ring (KF ring) is an orange, brown, or green-brown peripheral corneal discoloration secondary to gradual copper accumulation at the level of the Descemet membrane, adjacent to the limbus. It is significant for its presentation in patients with Wilson disease. It is clinically benign but may serve as a valuable screening and diagnostic aid (Brewer 2001; Copeland and Afshari 2013).

Etiology

The KF ring in Wilson disease is a result of systemic copper excess and is associated with autosomal recessive mutations in the *ATP7B* gene. This gene codes for an ATPase in the liver that transports copper into bile for excretion and incorporates it into ceruloplasmin, to be released into the bloodstream. In Wilson disease, copper accumulates in the liver and is released into the bloodstream in a free form not bound to ceruloplasmin. This free form is then deposited in the basal ganglia, kidneys, and eyes. This systemic accumulation manifests as tremor and rigidity in the central nervous system, renal tubular defects, and, in the eyes, KF ring and "sunflower" cataract formation.

Patients homozygous for the *H1069Q* mutation in *ATP7B* are more likely to demonstrate the KF ring; patients with Wilson disease due to this mutation tend to be diagnosed at an older mean age than patients heterozygous or negative for *H1069Q*.

Other etiologies for KF ring formation include primary biliary cirrhosis, progressive intrahepatic cholestasis of childhood, and chronic active hepatitis. Corneal chalcosis (corneal copper deposition) may also occur due to intraocular foreign body, chronic copper poisoning, and multiple myeloma (Smolin and Thoft 2005; Jankovic and Tolosa 2007; Suvarna 2008).

Occurrence

In the cornea, copper accumulation begins peripherally at Schwalbe's line and moves centrally; therefore, gonioscopy may be helpful to locate the ring in its early stage due to its primary peripheral location. The KF ring appears initially in superior and inferior corneal arcs which eventually coalesce to form a 1–3 mm wide, 360°, green-brown zone of copper granule deposits at the level of the Descemet membrane. It is generally bilateral but can present unilaterally if circulation to one eye is affected.

The KF ring is the most characteristic ocular feature in 95% of Wilson disease patients with neurological symptoms. These rings may be present in 50–60% of non-neurologically symptomatic disease and 10% of asymptomatic siblings. Additionally, "sunflower" cataracts may be present in 1 in 5 patients with neurologically symptomatic Wilson disease due to copper deposition in the lens capsule.

In addition, the KF ring may present as the earliest detectable manifestation of Wilson

disease, allowing this sign to serve as a useful screening and diagnostic tool. Examination for the KF ring is part of a screening test in first-degree relatives of affected individuals. In a patient with neurologic and/or psychiatric symptoms of Wilson disease, the presence of the KF ring provides diagnostic certainty. In presymptomatic patients, the KF ring may be present in 30–40% of cases, providing diagnostic certainty. In a patient with unexplained central nervous system disease, psychiatric disorder, deranged liver function tests, chronic active hepatitis, liver cirrhosis, rickets, renal tubular acidosis, or Coombs-negative hemolytic anemia, particularly with a family history of disease, the presence of a KF ring necessitates diagnostic workup (Brewer 2001; Smolin and Thoft 2005; Jankovic and Tolosa 2007; Suvarna 2008; Copeland and Afshari 2013).

Classification

Once diagnosed and identified, the size and intensity of a KF ring may serve as an indicator to classify responsiveness to treatment of Wilson disease. The magnitude of the ring may regress with administration of chelating therapy or following liver transplantation. The KF ring may serve as a monitoring tool for treatment compliance, though not as a prognostic marker (Brewer 2001; Smolin and Thoft 2005; Jankovic and Tolosa 2007; Suvarna 2008; Copeland and Afshari 2013).

Cross-References

► Wilson Disease

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KC

► Keratoconus

Kearns Syndrome

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Synonyms

Chronic progressive external ophthalmoplegia plus disease; Kearns-Sayre syndrome (KSS); Oculocraniosomatic disorder; Oculocraniosomatic neuromuscular disorder with ragged red fibers

Definition

It is a mitochondrial neuromuscular disorder affecting multiple parts of the body, classically the eyes and heart.

Etiology

KSS is the result of deletions in mitochondrial DNA. These mutations occur spontaneously in the majority of cases but mitochondrial, autosomal dominant, and autosomal recessive inheritance patterns have been documented. KSS is considered a form of chronic progressive external ophthalmoplegia (CPEO) with additional features. Mitochondrial DNA deletions are larger in KSS than in CPEO without additional features.

Clinical Presentation

The classic triad of KSS includes chronic progressive external ophthalmoplegia (CPEO), pigmentary retinopathy, and cardiac conduction defects. CPEO is a spectrum of clinical findings that include bilateral, slowly progressive ptosis and ophthalmoplegia of the extraocular muscles. Patients can be male or female and symptoms generally appear before the age of 20. Ptosis is the most common initial symptom; however cases have been reported with no ptosis. The condition is generally painless, pupils are spared, and patients rarely develop diplopia. The ophthalmoplegia includes vertical and horizontal gaze with no response to oculocephalic maneuvers; however, down gaze can be partially spared. Patients often adjust to their symptoms with a chin-up head tilt and by using the frontalis muscle to help elevate the eyelids.

Pigmentary retinopathy changes are often referred to as "salt and pepper fundus" and tend to be in the posterior pole. Cardiac problems can occur at any time but ptosis and ophthalmoplegia usually precede them. Complete heart block and sudden cardiac death can occur. A variety of other symptoms have been less commonly associated with KSS, including neurologic abnormalities (i.e., ataxia, hearing loss), somatic muscle weakness, endocrine abnormalities (i.e., hypoparathyroidism, gonadal dysfunction, diabetes mellitus), and other cardiac and ocular abnormalities.

Diagnosis

The diagnosis of KSS is made based on clinical findings. Attention should be focused on ruling out other underlying conditions. There is no specific laboratory test for KSS although some laboratory tests may aid in diagnosis including elevated CSF protein, elevated pyruvic acid, elevated creatine phosphokinase, elevated aldolase, cytochrome C oxidase deficiency, and elevated lactate in CSF and serum. Low magnesium and parathyroid hormone levels have also been reported. Limb and extraocular muscle biopsies may show ragged red fibers on light microscopy with Gomori trichrome stain. Mitochondrial testing can also be performed.

Differential Diagnosis

The differential diagnosis includes neuromuscular junction disease (e.g., myasthenia gravis, botulism), Eaton-Lambert syndrome, inflammatory disease (e.g., thyroid eye disease, idiopathic orbital myositis), infective myositis, neoplasm, infiltrative myopathy (e.g., sarcoidosis, amyloidosis), neurologic disorders (e.g., progressive supranuclear palsy), metabolic disease (e.g., primary cytochrome C oxidase deficiency, carnitine deficiency), Friedreich ataxia, Pierre-Marie disease, and spinocerebellar ataxia.

Prophylaxis

No prophylactic treatment is available. Genetic counseling may be offered.

Therapy

Regular evaluation by a cardiologist is important, and pacemaker implantation may be required in patients with KSS. No medical therapy has been proven to benefit patients with KSS although various treatments (coenzyme Q10, riboflavin, ketogenic diets) have anecdotal success. Steroids should be avoided, if possible as their use has been associated with fatal hyperglycemic metabolic acidosis with respiratory failure in patients with KSS. Supportive therapies for ocular manifestations include adhesive tape or lid crutches for ptosis, lubricants, and eye patch or goggles to prevent exposure keratitis. Possible surgical procedures include frontalis sling for ptosis, strabismus surgery for head tilt, and punctum occlusion for exposure keratitis.

Prognosis

KSS is a progressive disease with no known cure. Potential complications include sudden death from heart block, exposure keratitis, corneal ulceration, and visual loss.

Epidemiology

The prevalence of KSS is approximately 1–3 per 100,000 individuals. Symptom onset is usually before 20 years of age and may occur in infancy. Males and females are equally affected. There is no predilection for race.

Cross-References

▶ Chronic Progressive External Ophthalmoplegia Plus Disease

Further Reading

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Kearns-Sayre Syndrome (KSS)

▶ Kearns Syndrome

Keloids: Corneal and Congenital

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Synonyms

Corneal keloid

Definition

Overgrowth of the fibrous tissue beyond the normal limits that clinically appear as white raised gray-white mass involving the cornea. It often occurs secondary to traumatic or inflammatory reaction. However, it may also occur spontaneously such as in congenital keloids.

On histologic examination, keloid can be differentiated into two different stages. The early inflammatory stage is characterized by increase in vascularity and growth of fibroblasts that leads to the formation of collagen type III fibrils. The later fibrous stage is characterized by reduction of vascularity and fibroblasts with the formation of the densely packed collagen type I.

Character range of chapter: about 1 sentence to a quarter page, 500 characters the most

Few genetic syndromes have been associated with corneal keloid. These include Lowe syndrome and Rubinstein-Taybi syndrome. Furthermore, it has been noted that keloid tends to occur most commonly at the first two decades of life.

Management of corneal keloid can be challenging as it tends to recur after surgical correction. Current treatment modalities include superficial keratectomy, lamellar keratoplasty, or penetrating keratoplasty.

Cross-References

► Corneal Degenerations

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Kenacort-A

► Intravitreal Triamcinolone

Kenalog

► Intravitreal Triamcinolone

Kenaquart

► Intravitreal Triamcinolone

Keratectasia

► Corneal Ectasia
► Ectasia, Corneal
► Staphylomas, Congenital, Anterior

Keratectomy

► Corneal Ablation

Keratinocytes: Overview

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Synonyms

Basal keratinocytes; Corneocytes; Cornified keratinocytes; Granular keratinocytes; Horn cells; Spinous keratinocytes; Squamous cells (James et al. 2011; Adkinson et al. 2014)

Definition

Keratinocytes are the principal cells of the epidermis, derived from the ectoderm, whose main function is to produce keratin and provide a physical and immunological barrier against the outside environment (James et al. 2011).

Structure

Keratinocytes are the most abundant cell in the epidermis (90%) with a life cycle of approximately 28 days. They are continually renewing cells that can be divided into four types based on the epidermal layer in which they exist: basal, spinous, granular, and cornified. Basal keratinocytes are attached to the basement membrane by hemidesmosomes. A change in keratin composition of these cells precedes their differentiation into spinous keratinocytes, so named for their unique keratin cytoskeleton. The expression of lamellar granules containing the precursors of lipids present in the stratum corneum precedes conversion to granular cells. Granular

keratinocytes precede the stage before terminal differentiation and release their lipid contents to form the cornified lipid envelope (CLE) layer. Cornified keratinocytes are terminally differentiated cells that form the stratum corneum (Adkinson et al. 2014). This layer of cells lends the skin of terrestrial mammals its characteristic appearance (Bolognia et al. 2012).

The process described above is called keratinization, a differentiation process that terminates in cells known as cornified keratinocytes, corneocytes, or horn cells. Differentiation is triggered by a Ca^{2+} gradient that progresses through the layers of the epidermis, increasing steadily from the basal layer to the corneal layer. Keratinocyte stem cell differentiation culminates in cells that have replaced their plasma membrane with the cornified cell envelope (CE), a plethora of cross-linked proteins that lend the epidermis its characteristic appearance. These proteins include desmosomes, filaggrin, repetin, elafin, periplakin, envoplakin, cystatin, loricrin, small proline-rich proteins, late envelope proteins, and involucrin, among others (Bolognia et al. 2012). The cornified cell envelope is coated by lipids, which form the cornified lipid envelope (CLE). Terminally differentiated keratinocytes are flattened cells that have assembled the CE/CLE complex, have a keratin cytoskeleton, and have lost all of their organelles and nucleus. Though corneocytes are dead cells filled with protein, they play an active role in maintaining skin morphology and in carrying out its characteristic functions (Bolognia et al. 2012).

The main function of keratinocytes is to produce keratin, which is primarily a structural protein. There are 54 genes that code for keratin that is divided into two families: Type 1 (acidic) and Type 2 (basic). Different epithelial tissues express a specific keratin profile in a manner specific to tissue function. Type 1 and Type 2 keratins form coiled coil dimers that are the building blocks of the α-helical intermediate filament. Keratin coiled coil dimers are assembled into a complex pattern of parallel and antiparallel protofilaments and protofibrils. Keratohyalin is a proteinaceous substance that contributes to the soft, flexible nature of keratin. Hard keratin in the skin and nails lacks keratohyalin, and these tissues express keratins that contain large amount of cysteine that allows for the formation of cross-links to strengthen the cytoskeleton (James et al. 2011). Desmosomes provide an attachment site for the binding of the keratin cytoskeleton of keratinocytes and are also the key proteins involved in cell-to-cell adhesion (Calonje et al. 2012).

Function

Keratinocytes are critical in maintaining the barrier functions of the epidermis, including protection against pathogens and water loss. In the corneal layer of the epidermis, the formation of glutamyl-lysyl isopeptide bonds between CE proteins of the corneocyte by transglutaminase creates a watertight barrier. Desmosomal proteins are also cross-linked in this layer, adding further strength to the skin barrier. In the granular layer, keratin proteins, which represent most of the mass of the epidermis, are responsible for maintaining the epidermal barrier. Filaggrin proteins are a major component of keratohyalin and allow for the aggregation of keratin filaments (Calonje et al. 2012).

Along with serving a structural role in the epidermis, keratin is also involved in signaling. Keratin signaling is involved in both differentiation of keratinocytes and in basic cell functions such as apoptosis, metabolic activity, cell cycle progression, and the stress response. Keratinocytes coordinate this signaling activity by binding to signaling proteins in the cell (Bolognia et al. 2012).

Clinical Relevance

Keratinocytes, as part of the epidermis, are the first barrier in the body's defense against pathogens. They are essential for immune function, and if there is physical, chemical, or radiant energy insult to the skin, pathogens can invade the organism. Keratinocytes play a critical role in

immune function of the skin by participating in both the innate (constitutive and inducible) and adaptive immune response. Tight junctions between the cells form an impenetrable surface, and shedding of corneocytes allows for the shedding of superficial pathogens on the skin surface. The dryness of the cornified keratinocytes provides a relatively unfavorable environment for pathogenic growth. Keratinocytes also contain IgM antibodies and antimicrobial proteins such as defensins. The inducible innate response is initiated by the release of cytokines such as IL-1α and TNF-α that mediate a signaling cascade that culminates in acute inflammation. Keratinocytes are also amateur antigen-presenting cells that express major histocompatibility complex (MHC) Class II and integrin proteins and are key players in the induction of an adaptive immune response, particularly to allergens (James et al. 2011). Keratinocytes also release cytokines that attract dendritic cells and that help initiate a Th2 immune response (Adkinson et al. 2014).

Mutations in the genes that encode CE proteins, filaggrins/keratohyalins, and especially keratins can lead to skin disease. A few key examples are listed. Mutations in the loricrin and filaggrin genes can cause palmoplantar keratoderma (PPK) and ichthyosis vulgaris (Bolognia et al. 2012). Mutations in the genes that encode keratins 5 and 14 can lead to epidermolysis bullosa simplex. Mutations in the genes that encode keratins 1 and 10 can contribute to epidermolytic hyperkeratosis (James et al. 2011). Deletion of the entire keratin gene complex in mice was shown to be lethal (Bolognia et al. 2012). Additionally, defective keratinization can lead to skin abnormalities such as parakeratosis (retained nuclei), as corps ronds (round, clear to pink, abnormal cells), or as grains (elongated, basophilic, abnormal cells) (James et al. 2011).

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Keratinoid (Spheroidal) Degeneration

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Synonyms

Keratinoid corneal degeneration was a name originally proposed to describe the histologic appearance of abnormal proteins resembling prekeratin in corneal specimens from patients with globular deposits in the cornea (Garner 1970). Later reports disputed the evidence that this represented a keratinoid change and this entity fits the classification of the clinical term "spheroidal degeneration" (Fraunfelder and Hanna 1973). Several other reported clinical entities describe globular deposits of the cornea that may represent the same condition, with geographic variations or subtypes:

Band-shaped keratopathy; Band-shaped nodular dystrophy of the cornea; Bietti corneal degeneration; Chronic actinic keratopathy; Climatic droplet keratopathy; Colloid degeneration of the cornea; Degeneratio hyaloidea grannuliformis corneae; Elastoid degeneration; Elastotic degeneration; Eskimo corneal degeneration; Fisherman's keratopathy; Hyaline corneal degeneration; Keratoid corneal degeneration; Labrador keratopathy; Nodular corneal dystrophy in tropical arid countries; Nodular hyaline; Proteinaceous corneal degeneration; Sphaerularis elaiodes; Spheroid degeneration; Spheroidal keratopathy; Superficial central primary degeneration oleogutta; The blindness of Dahalach

Definition

A degeneration of the cornea and/or conjunctiva characterized by the appearance of golden yellow spherules or globules of varying size at or beneath the epithelium.

Etiology

The exact source of the protein material forming the spherules is unknown. It has been postulated that the material may result from the actions of ultraviolet light on serum proteins that diffuse into the cornea from limbal vessels (Farjo and Sugar 2009). Age and exposure to ultraviolet light are the most common associated factors. Other proposed risk factors include dry eyes, corneal trauma or microtrauma (wind, sand, ice), low humidity, and extremes of temperature. Associated ocular diseases include keratitis, lattice corneal dystrophy, and glaucoma (Fraunfelder and Hanna 1973).

Clinical Presentation

Spheroidal degeneration is characterized by the presence of yellow or golden spherules at or beneath the corneal or conjunctival epithelium. The spherules, or globules, are generally clear but may become more opaque over time and range in size from approximately 0.1 to 0.6 mm in diameter. These lesions are located in the superficial corneal stroma, bowman membrane, subepithelium, and occasionally in the epithelium in advanced degeneration (Magovern et al. 2004).

The clinical presentation has been described as either a primary corneal type associated with age, a secondary corneal type associated with other ocular pathologies, or a conjunctival form that may or may not be associated with either type of corneal degeneration (Fraunfelder and Hanna 1973). In the primary form, the lesions are typically seen at the horizontal limbus within the palpebral fissure, and with progression, the spherules enlarge and spread toward the central cornea. In the secondary corneal form, the lesions are less likely to assume a band-shaped configuration and may be concentrated around areas of prior scarring, neovascularization or inflammation. The lesions are generally bilateral except in secondary cases where there is associated unilateral pathology such as scars, trauma, or keratitis. In the conjunctival form, lesions occur interpalpebrally at the 3 and 9 o'clock positions and are frequently found in association with pinguecula.

Diagnosis

Diagnosis is made clinically based on the characteristic appearance. Biopsy with histologic examination can support or confirm the diagnosis but is not typically required. Histologically, deposits appear as extracellular amorphous globules, which may coalesce to form larger masses in Bowman's membrane (Farjo and Sugar 2009).

Differential Diagnosis

Similar appearing clinical entities include corneal amyloid degeneration, gelatinous drop-like corneal dystrophy (familial subepithelial amyloidosis), band keratopathy, climatic proteoglycan stromal keratopathy, primary lipoidal degeneration of the cornea, Salzmann nodular degeneration, and limbal girdle of Vogt (type II).

Prophylaxis

Unknown. Based on the recognized association with sunlight exposure, it is plausible that methods to reduce sunlight exposure could potentially reduce the development or progression of spheroidal degeneration.

Therapy

Treatment is rarely required since the majority of individuals are asymptomatic. In patients with loss of vision from central corneal lesions, treatment can be considered. Possible treatment

options include superficial keratectomy, phototherapeutic keratectomy, lamellar keratoplasty, or penetrating keratoplasty depending on the depth and density of the lesions.

Prognosis

The majority of individuals do not develop any symptoms and progression is slow in the primary form. However, progression may result in loss of vision, particularly in areas of the world where climatic exposure is severe. Visual acuity may be affected due to involvement of the visual axis of the cornea or from irregular astigmatism. In advanced disease, accumulation of globular masses or plaques may cause heaping up of the corneal surface, epithelial defects, and recurrent corneal erosions. Corneal sensation may be reduced and sterile ulceration may rapidly progress to microbial keratitis or perforation.

Epidemiology

The prevalence of spheroidal degeneration varies based on geographic location with rates of 6% in England and over 60% in males in Labrador (Farjo and Sugar 2009). It is approximately three times more common in males and increases with age, being found in roughly 50% of patients over 70 years of age (Fraunfelder and Hanna 1973). It is most frequently seen in areas with high sunlight exposure. While the primary form is generally considered a degeneration, there are rare reported cases describing a more dystrophic form that may be familial and occurs in relatively young patients without a history of other ocular disease or environmental exposure (Santo et al. 1993).

Cross-References

- ▶ Climatic Droplet Keratopathy (Spheroidal Degeneration)
- ▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
- ▶ Spheroidal Degeneration

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Keratinoid Corneal Degeneration

▶ Spheroidal Degeneration

Keratitis

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Synonyms

Corneal inflammation

Definition

Keratitis may be caused by noninfectious agents or from exposure to or invasion by infectious organisms. Keratitis in general can affect all layers of the cornea.

Histology

Histological studies in some cases help in finding the underlying cause for keratitis. A granulomatous

reaction against Descemet's membrane can be seen in herpetic stromal keratitis, while a loss of keratocytes in the anterior part of the stroma is found in neurotrophic keratitis. In acanthamoeba keratitis, corneal edema, loss of Bowman's membrane, and inflammatory infiltrate consisting of leucocytes can be present in the superficial corneal stroma. Amoeba oocysts can be stained and is found in the deeper layers of the stroma (Cursiefen and Kruse 2007; O'Brien 2005).

Immunohistochemistry

To differentiate between acanthamoeba and viral keratitis, and in some cases, between immunological disorders such as Terrien's or Mooren's ulcer, immunohistochemistry is employed (Lopez et al. 1991).

Electron Microscopy

Electron microscopy has been used to demonstrate the structure of the viral particles of herpes simplex, bacterial structures, and acanthamoeba as well as the affected corneal layers.

Molecular Diagnosis

To differentiate between various infectious agents, polymerase chain reaction (PCR) is available.

Differential Diagnosis

Infectious causes: Bacterial/viral/fungal/acanthamoeba keratitis.

Noninfectious: filamentary/superficial punctuate/photoelectric/neurotrophic/immunologic (phlyctenular and staphylococcal)/autoimmune keratitis.

Cross-References

- ▶ Bacterial Keratitis
- ▶ Candida Keratitis/Ocular Infection
- ▶ Exposure Keratitis/Keratopathy
- ▶ Interstitial Keratitis
- ▶ Lamellar Keratoplasty
- ▶ Mooren Ulcer
- ▶ Stromal Keratitis (Herpetic)
- ▶ Terrien Marginal Degeneration
- ▶ Thygeson's Superficial Punctate Keratitis

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Keratitis Disciformis

- ▶ Disciform Keratitis, Herpes Simplex Virus Causing

Keratitis Sicca

- ▶ Keratoconjunctivitis: Overview

Keratoacanthoma

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Synonyms

Molluscum sebaceum

Definition

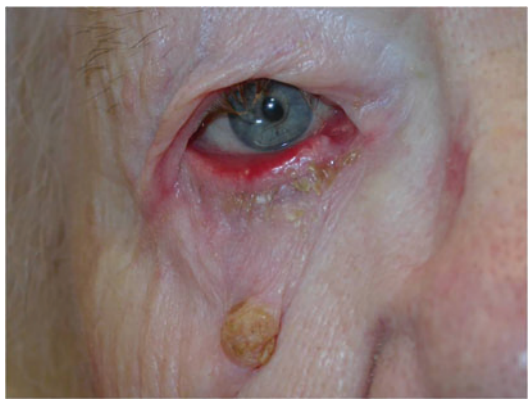
A skin tumor characterized by a very rapid growth phase, followed by gradual involution. Some consider keratoacanthoma (KA) a subtype of squamous cell carcinoma. The tumor is most commonly seen on sun-exposed areas and in white elderly patients. Males are more often affected than females (Leibovitch et al. 2005; Albert and Jakobiec 2008; Shields and Shields 2008).

Etiology

Unclear, however, several potentiating factors should be considered such as trauma, exposure to chemical agents, human papilloma virus infection, and immunocompromised status. Keratoacanthomas may also develop after laser resurfacing, radiation therapy, and at the donor site after skin grafting (Albert and Jakobiec 2008; Shields and Shields 2008).

Clinical Presentation

The classical appearance is a well-defined, solitary, firm, skin-colored, or reddish papule that rapidly progress to dome-shaped nodule, with central keratotic crater and elevated rolled margins (Fig. 1). Usually solitary lesions; however, there are a number of syndromes that feature multiple keratoacanthomas, including the Muir-Torre syndrome, a generalized eruptive variant of Grzybowski, and the Ferguson Smith syndrome. Multiple keratoacanthomas may be associated with visceral malignancies (Albert and Jakobiec 2008; Shields and Shields 2008).



Keratoacanthoma, Fig. 1 Keratoacanthoma in malar area of an elderly man

Diagnostics

Despite KA's distinctive morphological features, differentiation from invasive SCC can only be made histologically. A biopsy should be obtained in order to establish a definitive diagnosis (Leibovitch et al. 2005; Albert and Jakobiec 2008; Shields and Shields 2008).

Differential Diagnosis

Differential Diagnosis includes ▶ basal cell carcinoma, ▶ squamous cell carcinoma, ▶ actinic keratosis, ▶ inverted follicular keratosis, and ▶ molluscum contagiosum.

Prophylaxis

Avoidance of sun and UV exposure (use of sunscreens, sunglasses, umbrellas, and hats).

Therapy

KA may regress spontaneously over a period of 3–6 months. Observation of periocular KA carries some risk, especially when histologic differentiation is important to rule out malignancy. The primary therapy is surgical excision of the tumor with frozen section control. It is essential not only to maintain normal eyelid function but also to prevent further tissue destruction and invasion into deeper tissues.

Prognosis

KA infrequently presents as multiple tumors and may enlarge (5–15 cm), become aggressive locally, or rarely, metastasize.

Epidemiology

Uncertain.

Cross-References

- ▶ Actinic Keratosis
- ▶ Basal Cell Carcinoma of Eyelid
- ▶ Inverted Follicular Keratosis
- ▶ Molluscum Contagiosum
- ▶ Squamous Cell Carcinoma of Eyelid

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Keratoconjunctivitis Sicca

- ▶ Dry Eye: Definition

Keratoconjunctivitis Sicca (KCS)

- ▶ Keratoconjunctivitis: Overview

Keratoconjunctivitis, Sicca: Definition

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Synonyms

Dry eye disease

Definition

Keratoconjunctivitis sicca is defined as a multifactorial disease of the tears and ocular surface that leads to discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. The disease is often accompanied by increased osmolarity of the tear film and inflammation of the ocular surface (Nassiri et al. 2011). Dry eye disease is far from just a dysfunction of the lacrimal glands. It is a result of dysfunction of the complex interplay of factors involving the lacrimal glands, lids, ocular surface, lacrimal drainage ducts, medications, contact lens wear, and the environment (Lemp 2005).

The tear film is composed of three components. There is a mucin layer, aqueous layer, and lipid layer. These components work together to maintain a normal ocular surface in health and repair in response to injury. The tear film also forms the anterior refracting surface of the eye. Thus, a dysfunctional tear film degrades the visual image perceived by the retina and compromises visual acuity. The tear film also provides hydration to the ocular surface and functions as a lubricant between the eyelid and ocular surface. Studies have shown that tear films break up prior to the next blink in patients with keratoconjunctivitis sicca. In keratoconjunctivitis sicca, the tear film is disrupted, leading to symptoms varying from irritation to severe pain. The discomfort of dry eye disease has been described as dryness, grittiness, stinging, foreign body sensation, itching, burning, and stinging (Lemp 2005).

Two main divisions of keratoconjunctivitis sicca are aqueous tear deficiency and evaporative tear deficiency. Over 60% of patients with Sjogren's syndrome associated keratoconjunctivitis sicca have both forms of dry eye. Additionally, many of the patients with severe forms of keratoconjunctivitis sicca have evidence of Sjogren's syndrome (Lemp 2005).

The prevalence of clinically diagnosed dry eye disease in the United States is 0.4–0.5%, highest amongst women and the elderly (Nassiri et al. 2011). Age-related changes in the lacrimal and meibomian gland functions have been reported. The correlation with advancing age and

changes in hormone status suggests that sex hormones may be involved in the maintenance of tear secretion (Lemp 2005). Tens of millions of individuals have a less severe form of the disease that may be episodic, occurring only during adverse conditions, such as contact lens wear and low humidity. Due to its significant prevalence, keratoconjunctivitis sicca is considered a significant public health issue, which will have a considerable economic impact (Nassiri et al. 2011).

The mainstay of treatment has been palliative with lubricant eye drops and artificial tears. However, the US Food and Drug Administration has approved cyclosporine-A (Restasis-Allergan) for the treatment of keratoconjunctivitis sicca. Systemic food supplements, such as flax seed oil and omega-3 fatty acids, are in wide use. They may function by suppressing inflammation and contributing to the synthesis of lipids of the meibomian glands (Lemp 2005).

Cross-References

▶ Meibomian Glands

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Keratoconjunctivitis: Overview

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Synonyms

Dry eye; Dry eye syndrome; Keratitis sicca; Keratoconjunctivitis sicca (KCS); Sicca syndrome; Tear deficiency

Definition

An insufficient tear film to maintain ocular surface health, comfort, or luster required for optimal visual acuity.

Etiology

The pathogenesis is multifactorial, but is broken down into aqueous deficiency (inadequate lacrimal gland function) and increased evaporative state (insufficient lipophilic tear layer which normally prevents aqueous tear evaporation) (2007). Aqueous deficiency may be related to normal aging, hormonal imbalances, collagen vascular disease, autonomic neuropathy, systemic or local inflammatory conditions, systemic medications, or vitamin deficiency. Increased evaporative states may be caused by blepharitis (meibomitis especially), ineffective blinking or abnormal lid anatomy (ectropion), topical medications, contact lens wear, or surface inflammation.

Clinical Presentation

Patients typically present with ocular irritation (foreign body sensation, itching, burning, dryness) and fluctuating visual accuity that is often improved by blinking (Goren and Goren 1988). Redness, mucoid discharge, epiphora (from reflex tearing), and photophobia might also be seen.

Diagnosis

Numerous tests may aid in the diagnosis such as tear film breakup time (BUT), Schirmer testing, corneal vital staining, tear osmolarity, and tear immunoassays for lactoferrin and lysozyme. However, all these tests suffer from less than ideal predictive values. Diagnosis is best made by history and a careful slit lamp examination of the quality of the tear film and adnexal structures. Blood tests may be used to diagnose underlying systemic inflammatory conditions resulting in secondary dry eye.

Differential Diagnosis

The differential diagnosis of KCS is extensive and includes all forms of blepharitis, lid malpositions, infectious keratoconjunctivitis, ocular allergy, medicamentosa, and other forms of keratitis and degenerative keratopathies.

Prophylaxis

Avoidance of known precipitators can help. Daily warm compresses keep meibomian orifices open in evaporative dry eye. Avoidance of dry environments and humidifiers are useful. Alternative medications that do not cause drying if possible is of benefit.

Therapy

Therapy depends on underlying cause (Behrens et al. 2006). For evaporative states associated with meibomitis, warm compresses, lid hygiene, and systemic medications like tetracyclines or azolides can be useful. For aqueous-deficient states, the mainstay of treatment is artificial teardrops. Punctal occlusion is extremely useful and probably underutilized. Topical cyclosporin and steroids may be of use in inflammatory states. Oral omega-3 fatty acids have been shown to be of benefit. Autologous serum eye drops are useful in the most severe cases. Chronic treatment is generally required and relapses expected with discontinuation of treatment.

Prognosis

Mild to moderate KCS is generally controllable with therapeutic intervention and these patients will function normally. More severe cases, however, can cause significant morbidity and seriously impact quality of life. Severe KCS may result in profound vision loss and secondary corneal infection which can threaten vision and the integrity of the globe; fortunately, these cases are far more rare.

Epidemiology

The classic KCS patient is a postmenopausal female, but this condition can occur in either sex and at any age (2007). The exact prevalance of this condition is unknown, but it is estimated that between 10% and 30% of the population (more so in older groups) is affected. Females are affected over men approximately 2:1. KCS associated with autoimmune disease is far more common in women.

Related Entries

Blepharitis, Blepharoconjunctivitis, Conjunctivitis, Dry Eye, Keratoconjunctivitis sicca, Diagnostic Procedure, Goblet Cells, Lagophthalmos, Meibomian Gland Dysfunction, Precorneal Tear Film, Schirmer Tests, Tear Breakup Time

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Keratoconus

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Synonyms

KC

Definition

An ectatic, noninflammatory corneal dystrophy leading to progressive corneal thinning with subsequent development of irregular astigmatism (higher-order aberrations) and decrease of best-corrected visual acuity. The name is derived from the cone shape of the cornea at later stages of the disease.

Etiology

While there is evidence for formal pathogenetic mechanisms, the underlying etiology is unknown yet. Immunohistochemistry uncovered different expression patterns of α_1-proteinase inhibitor and matrix metalloproteinases (MMP) in normal and KC eyes. KC showed lower levels of α_1-proteinase inhibitor and higher levels of MMP-1 compared to normal eyes (Cristina Kenney and Brown 2003; Meghpara et al. 2008; Balasubramanian et al. 2010). Apart from a multifactorial hereditary component, severe eye rubbing is still discussed as one etiologic risk factor (Carlson 2010), which is suggested by clinical experience with patients with Leber's congenital amaurosis or Tourette's syndrome (Mashor et al. 2011). A study involving a multivariable analysis did not confirm atopic diathesis itself (another condition known to be associated with KC) but eye rubbing, which is often present, as a risk factor for KC (Bawazeer et al. 2000).

Clinical Presentation

Typical early signs and symptoms include blurry vision, myopization, increase of astigmatism, a difficult subjective refraction, and loss of best-corrected visual acuity. Later, corneal abnormalities can be detected at the slit lamp. The earliest of these slit-lamp signs is a pronounced reflex of the endothelium, followed by vertical striae of Descemet's layer (Vogt's striae). At later stages, corneal scarring, corneal hydrops (often referred to as "acute KC"), and the eponymous cone-like shape of the cornea can be observed.

Diagnostics

The gold standard for the diagnosis of KC is corneal topography. Corneal topographic maps of KC eyes show typical characteristics like and asymmetric bow-tie pattern, skewed radial axes, or a centralized ("baby") bow-tie pattern. In the early (subclinical) stage of the disease, these signs are often very subtle and may be overlooked, particularly in asymptomatic patients. Later, with progression of the disease, corneal curvature increases significantly with the typical patterns still present. Metrics computed from corneal topographic data can help to establish the diagnosis of KC in doubtful cases (Maeda et al. 1995; Rabinowitz 1995; Bühren et al. 2010). Newer approaches also use Scheimpflug tomography (Bühren et al. 2010; Ambrosio et al. 2011) or elastometry (Fontes et al. 2011). In default of corneal topography, streak retinoscopy is a very sensitive tool for the detection of early KC forms.

Differential Diagnosis

High regular astigmatism, pellucid marginal degeneration, iatrogenic keratectasia, keratoglobus, and *status post* hyperopic LASIK.

Prophylaxis

There is no established prophylaxis against KC. With eye rubbing getting more into the focus as a significant risk factor, a prevention of pathological eye rubbing could play a role in the future.

Therapy

The gold standard is the correction of myopia, astigmatism, and higher-order aberrations (HOA) in KC eyes with rigid gas-permeable contact lenses (RGPs), often special RGPs for KC eyes. RGPs allow a satisfactory visual acuity for a long time. If RGPs are not tolerated; a correction at least of lower-order aberrations can be achieved with glasses. Newer surgical therapies are the

implantation of ring segments into the cornea in order to achieve a more regular corneal shape (Ertan and Colin 2007) or the implantation of a toric intraocular lens into the phakic eye in order to correct lower-order aberrations (Kato et al. 2011).

With the introduction of corneal collagen cross-linking (CXL), a more causative therapy beyond mere correction of optical aberrations became possible. Studies showed that the CXL treatment is able to halt the progression of KC (Hersh et al. 2011). Thus, the disease could be "frozen" at a stage when RGPs can still be worn by the patient and the necessity for keratoplasty as the *ultima ratio* treatment can be prevented or at least be delayed.

Keratoplasty is performed if the best-corrected visual acuity is low (typically >1.0 logMAR) due to corneal scarring and RGP intolerance. Newer developments include lamellar techniques that preserve the endothelium of the often young patients; however, penetrating keratoplasty is still the gold standard among the keratoplasty techniques for the treatment of KC.

Prognosis

If progression is slow and if RGPs are tolerated, the prognosis is excellent with patients reaching visual acuity values of around 0.1 logMAR. Patients who require keratoplasty may reach lower visual acuity values, particularly in case of high post-keratoplasty astigmatism, elevated HOA levels, and RGP intolerance.

Epidemiology

The medial prevalence is 55:100,000 with a proclivity for the male sex. However, inter-racial differences have been reported (Georgiou et al. 2004).

Cross-References

- ▶ Corneal Collagen
- ▶ Corneal Ectasia
- ▶ Corneal Topography
- ▶ Keratoglobus
- ▶ Pellucid Marginal Degeneration
- ▶ Stromal Degenerations

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Keratoectasia

▶ Corneal Ectasia
▶ Ectasia, Corneal

Keratoglobus

▶ Stromal Degenerations

Keratoglobus Basic Science

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Synonyms

Anterior megalophthalmus; Megalocornea

Definition

Keratoglobus is a rare, degenerative bilateral corneal disease characterized by corneal thinning and hemispherical protrusion that may lead to myopia (Lange and Gareis 2007).

Structure

Keratoglobus is characterized by thinning of the cornea from limbus to limbus (Wallang and Das 2013). Scleral thinning and minimal corneal scarring may also be involved. The cornea tends to be of normal or increased diameter with these physical changes (Karabatsas and Cook 1996). The eye will have normal to low intraocular pressure with a normal disk. Corneal edema is a rare complication of keratoglobus that increases the risk of rupture.

Functions

The cause of keratoglobus is unclear, and the pattern of corneal thinning tends to be unpredictable (Krachmer et al. 1984). Patients may report vision deterioration that affects their daily functioning. Keratoglobus does not cause blindness though.

Clinical Relevance

Keratoglobus is much more rare than keratoconus, the more common corneal dystrophy (Krachmer et al. 1984).

Keratoglobus exists in at least two forms: congenital juvenile and acquired adult form (Wallang and Das 2013). The congenital form presents at birth and has been associated with Ehlers-Danlos type VI, blue sclera syndrome, and Leber congenital amaurosis. The acquired form of keratoglobus presents in adulthood and has been associated with preexisting keratoconus, inflammatory orbital pseudotumor, chronic marginal blepharitis, and post-penetrating keratoplasty glaucoma. It has also been involved in cases of vernal keratoconjunctivitis and hyperthyroidism.

Patients typically present with bilateral visual impairment that does not correct with spectacles or contact lenses. Contact lenses may also be reported to have poor fit or associated with pain. Eye pain may occur in rare cases.

Clinical diagnosis is made using slit lamp exam. Physical exam signs associated with keratoglobus are myopia, irregular astigmatism, diffuse corneal thinning, globular protrusion of the cornea, corneal hydrops, and possible scarring.

Differential diagnosis includes keratoconus, pellucid marginal degeneration, and corneal ectasia following refractive surgery.

There are several avenues for treatment and management of keratoglobus. Spectacles are the first step for visual correction and protection. Success with contact lenses may be difficult due to the

abnormal corneal contours (Wallang and Das 2013). Further, the risk of trauma with continuous manipulation with contact lenses must be weighed. No medical therapy has been found to be effective in treating the underlying pathology of keratoglobus. Treatment of symptoms, such as hydrops, is necessary, with suggested methods being hypertonic saline or bandage soft contact lenses.

Surgical management may be necessary when vision improvement cannot be obtained otherwise. Lamellar epikeratoplasty has been successful in reinforcing thin corneas and improving vision (Jones and Kirkness 2001). Large penetrating keratoplasty has been found to be successful for acquired keratoglobus (Kodjikian et al. 2004). However, these procedures come with several complications, and success of the surgical intervention is not guaranteed.

The prognosis for keratoglobus is poor due to difficult response to spectacles and surgical interventions (Wallang and Das 2013).

Cross-References

- ▶ Corneal Ectasia
- ▶ Keratoconus
- ▶ Pellucid Marginal Degeneration

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Keratoid Corneal Degeneration

- ▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
- ▶ Keratinoid (Spheroidal) Degeneration
- ▶ Spheroidal Degeneration

Keratolimbal Autograft/Allograft

- ▶ Limbal Autograft/Allograft (Limbal Transplantation)

Keratolysis (Corneal Melting), Marginal, Systemic Immune-Mediated Disease

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Synonyms

Corneal melting; Peripheral ulcerative keratitis; Scleritis-associated peripheral keratopathy

Definition

Thinning of peripheral corneal stroma with an overlying epithelial defect due to autoimmune-induced inflammation.

Etiology

Systemic immune-mediated marginal keratolysis occurs in response to infectious and non-infectious insults. Infectious etiologies include bacteria species (*Staphylococcus* species, *Streptococcus* species, *Treponema pallidum*,

Mycobacterium tuberculosis), viruses (hepatitis C, herpes simplex virus, varicella zoster virus), *Acanthamoeba*, and fungi (Dana et al. 2000). Noninfectious causes include rheumatoid arthritis, Wegener's granulomatosis, relapsing polychondritis, polyarteritis nodosa, and systemic lupus erythematosus (Odorcic et al. 2009). One-third of peripheral ulcerative keratitis cases are associated with rheumatoid arthritis (Tauber et al. 1990).

Marginal keratolysis stems from the peripheral cornea's proximity to limbal vasculature. The capillary bed brings inflammatory cells and mediators in contact with the peripheral cornea, inducing inflammation. It has been theorized that corneal inflammation is due to both T-cell and antibody-mediated responses. T cells induce antibody formation and immune complex deposition in the peripheral cornea. Recruited neutrophils and macrophages secrete collagenases and proteases, which, in turn, destroy the peripheral cornea stroma (Dana et al. 2000).

Occurrence

The incidence is estimated to be three cases per million per year (Knox et al. 2013). Men and women are equally affected (Tauber et al. 1990).

Classification

Symptoms of keratolysis include eye pain, decreased visual acuity (from corneal opacification or astigmatism), redness, tearing, and photophobia. Signs include de-epithelialization, stromal thinning, cellular infiltration, and contiguous inflammation of surrounding conjunctiva and sclera. Thinning typically occurs in the peripheral cornea within 2 mm of the limbus and maintains a curvilinear shape. Corneal melting is a late complication of the disease. Progressive thinning of the cornea can lead to perforation.

Cross-References

- ▶ Cornea
- ▶ Corneal Collagen
- ▶ Corneal Limbus
- ▶ Corneal Stromal Haze
- ▶ Corneal Ulcers
- ▶ Epithelial Defects
- ▶ Keratitis

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Keratomalacia, Vitamin A Deficiency

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Definition

Keratomalacia is characterized by corneal melting, conjunctival xerosis, and in advanced disease, liquefactive necrosis of the corneal stroma. It is frequently associated with xerophthalmia secondary to vitamin A deficiency, is

generally bilateral, and is most commonly seen in malnourished children less than 5 years of age in developing countries. Its prevalence in economically advanced countries is rare but associated with metabolic, psychiatric, and eating disorders affecting vitamin A intake. Treatment should address reversal of vitamin A deficiency and improvement of general health; perforations may require corneal transplantation.

Cross-References

► Xerophthalmia

Keratomileusis

► Corneal Ablation

Keratomycosis

► Candida Keratitis/Ocular Infection

Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)

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Synonyms

Chronic actinic keratopathy describes a condition associated with conjunctival elastosis and typified by characteristic extracellular concretions (Klintworth 1972). A later publication found this and other entities, including Labrador keratopathy, to fit the classification of the clinical term "spheroidal degeneration" (Fraunfelder and Hanna 1973). Several other reported clinical entities describe globular deposits of the cornea that may represent the same condition, with geographic variations or subtypes:

Band-shaped nodular dystrophy of the cornea; Bietti corneal degeneration; Chronic actinic keratopathy; Climatic droplet keratopathy; Colloid degeneration of the cornea; Degeneratio hyaloidea grannuliformis corneae; Elastoid degeneration; Elastotic degeneration; Eskimo corneal degeneration; Fisherman's keratopathy; Hyaline corneal degeneration; Keratoid corneal degeneration; Labrador keratopathy; Nodular corneal dystrophy in tropical arid countries; Nodular hyaline, band-shaped keratopathy; Proteinaceous corneal degeneration; Sphaerularis elaiodes; Spheroid degeneration; Spheroidal keratopathy; Superficial central primary degeneration oleogutta; The blindness of Dahalach

Definition

A degeneration of the cornea and/or conjunctiva characterized by the appearance of golden yellow spherules or globules of varying size at or beneath the epithelium.

Etiology

The exact source of the protein material forming the spherules is unknown. The initial description suggested this condition was due to the effect of chronic actinic irradiation. It has since been postulated that the material may result from the actions of ultraviolet light on serum proteins that diffuse into the cornea from limbal vessels (Farjo and Sugar 2009). Age and exposure to ultraviolet light are the most common associated factors. Other proposed risk factors include dry eyes, corneal trauma or microtrauma (wind, sand, ice), low humidity, and extremes of temperature. Associated ocular diseases include keratitis, lattice corneal dystrophy, and glaucoma (Fraunfelder and Hanna 1973).

Clinical Presentation

Spheroidal degeneration is characterized by the presence of yellow or golden spherules beneath the corneal or conjunctival epithelium. The spherules, or globules, are generally clear but may become more opaque over time and range in size from approximately 0.1 to 0.6 mm in diameter. These lesions are located in the superficial corneal stroma, bowman membrane, subepithelium, and occasionally in the epithelium in advanced degeneration (Magovern et al. 2004).

The clinical presentation has been described as either a primary corneal type associated with age, a secondary corneal type associated with other ocular pathology, and a conjunctival form that may or may not be associated with either type of corneal degeneration (Fraunfelder and Hanna 1973). In the primary form, the lesions are typically seen at the horizontal limbus within the palpebral fissure, and with progression, the spherules enlarge and spread toward the central cornea. In the secondary corneal form, the lesions are less likely to assume a band-shaped configuration and may be concentrated around areas of prior scarring, neovascularization, or inflammation. The lesions are generally bilateral except in secondary cases where there is associated unilateral pathology such as scars, trauma, or keratitis. In the conjunctival form, lesions occur interpalpebrally at the 3 and 9 o'clock positions and are frequently found in association with pinguecula.

Diagnosis

Diagnosis is made clinically based on the characteristic appearance. Biopsy with histologic examination can support or confirm the diagnosis but is not typically required. Histologically, deposits appear as extracellular amorphous globules, which may coalesce to form larger masses in Bowman's membrane (Farjo and Sugar 2009).

Differential Diagnosis

Similar appearing clinical entities include corneal amyloid degeneration, gelatinous drop-like corneal dystrophy (familial subepithelial amyloidosis), band keratopathy, climatic proteoglycan stromal keratopathy, primary lipoidal degeneration of the cornea, Salzmann nodular degeneration, and limbal girdle of Vogt (type II).

Prophylaxis

Unknown. Based on the recognized association with sunlight exposure, it is plausible that methods to reduce sunlight exposure could potentially reduce the development or progression of spheroidal degeneration.

Therapy

Treatment is rarely required since the majority of individuals are asymptomatic. In patients with loss of vision from central corneal lesions, treatment can be considered. Possible treatment options include superficial keratectomy, phototherapeutic keratectomy, lamellar keratoplasty, or penetrating keratoplasty depending on the depth and density of the lesions.

Prognosis

The majority of individuals do not develop any symptoms and progression is slow in the primary form. However, progression may result in loss of vision, particularly in areas of the world where climatic exposure is severe. Visual acuity may be affected due to involvement of the visual axis of the cornea or from irregular astigmatism. In advanced disease, accumulation of globular masses or plaques may cause heaping up of the corneal surface, epithelial defects, and recurrent corneal erosions. Corneal sensation may be

reduced and sterile ulceration may rapidly progress to microbial keratitis or perforation.

Epidemiology

The prevalence of spheroidal degeneration varies based on geographic location with rates of 6% in England and over 60% in males in Labrador (Farjo and Sugar 2009). It is approximately three times more common in males and increases with age, being found in roughly 50% of patients over 70 years of age (Fraunfelder and Hanna 1973). It is most frequently seen in areas with high sunlight exposure. While the primary form is generally considered a degeneration, there are rare reported cases describing a more dystrophic form that may be familial and occurs in relatively young patients without a history of other ocular disease or environmental exposure (Santo et al. 1993).

Cross-References

- ▶ Climatic Droplet Keratopathy (Spheroidal Degeneration)
- ▶ Keratinoid (Spheroidal) Degeneration
- ▶ Spheroidal Degeneration

References

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Keratoprosthesis

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Synonyms

Artificial cornea; KPro

Definition

An artificially produced ophthalmic device meant to replace the natural cornea. These devices can be completely synthetic, hybrids of synthetic and natural materials, or completely composed of biologic materials.

Indication

There are three basic indications for keratoprostheses: corneal allograft failure, severe chemical injuries affecting the cornea, and severe autoimmune disease affecting the cornea. Not all of these indications apply to all of the various types of keratoprostheses (Chodosh and Dohlman 2011).

Contraindication

Some general contraindications include no light perception vision, posterior segment abnormalities, uncontrolled intraocular pressure, useful vision or functional keratoprosthesis in the fellow eye, eyelid or blink abnormalities, and poor access to ophthalmologist performing or familiar with procedure or poor commitment to frequent follow-up. Other contraindications that may or may not apply depending on the type of keratoprosthesis used include herpes simplex keratitis, autoimmune disorders, and age under 18 years (Chodosh and Dohlman 2011).

Techniques and Principles

Type 1 Boston Keratoprosthesis (BKPro)

The type 1 BKPro consists of four components: a polymethyl methacrylate (PMMA) optical front plate and stem, a corneal graft button with a central trephination, and a back plate and a titanium locking ring. Holes in the back plate allow for aqueous nutrition of the corneal button.

The device is assembled by placing the front plate and stem through a prepared corneal graft button with a central trephination. The back plate is then placed onto the stem and the entire assembly is secured using the titanium locking ring. The host cornea is then trephinated and the corneal graft button is then sutured to the host cornea as in a standard penetrating keratoplasty procedure (Fahd et al. 2013).

Osteo-odonto-keratoprosthesis (OOKP)

The OOKP consists of an optical cylinder held in the patient's tooth root and surrounding alveolar bone. This creates a bed for the optical element that supports the optical element while allowing for integration into the surrounding tissue in order to minimize the risk of extrusion.

Implantation consists of two stages. In the first stage, the patient's tooth is removed with adjacent bone and a hole is then drilled into the center of the tooth root. An optical cylinder is then cemented into the hole. This tooth-optic lamina complex is then implanted into a submuscular location (usually the lower eyelid). A 360-degree peritomy is then performed on the host eye, followed by removal of epithelium and Bowman's layer. A mucous membrane graft, most often obtained from the cheek, is secured to the exposed sclera. The tooth-optic lamina complex and the mucous membrane are left in place for 2–4 months, which allows for formation of a fibrovascular covering over the tooth-optic lamina complex and vascularization of the mucous membrane. In the second stage, the tooth-optic lamina complex is removed from the submuscular bed and a flap is then made in the mucous membrane that had previously been grafted to the sclera. The host cornea is then trephinated, and the lens and iris are removed followed by anterior vitrectomy. The tooth-optic lamina complex is then sutured to the host cornea and the mucous membrane graft is resutured in place. A hole is then cut in the central portion of the mucous membrane graft, exposing the optic (Gomaa et al. 2010; Fahd et al. 2013).

AlphaCor (TM)

The AlphaCor(TM) is made up of two different parts, both made of poly-2-hydroxyethyl methacrylate (pHEMA). This device consists of a central transparent optic and a porous, opaque outer skirt. The porous outer zone allows integration of keratocytes and blood vessels into the outer portion of the device.

Implantation of the AlphaCor(TM) occurs in two stages. In the first stage, a 360-degree peritomy is fashioned and the corneal epithelium is removed. A lamellar corneal flap is then constructed in the superior half of the cornea at approximately 50% thickness. Dissection is then carried through the inferior cornea creating a pocket in the inferior cornea. A trephine is then used to enter the anterior chamber in the middle of the posterior corneal layer. The AlphaCor (TM) device is then placed into the pocket in the inferior cornea and centered over the hole in the posterior cornea. The superior corneal flap is then sutured to the limbus. The second stage of the procedure occurs 8–12 weeks later, at which time the superficial corneal layer overlying the AlphaCor(TM) is trephinated exposing the clear optical zone of the device (Gomaa et al. 2010; Fahd et al. 2013).

Other Types of Keratoprostheses

In addition to the aforementioned types of keratoprostheses, a number of other types of keratoprostheses have been developed. These include the Seoul type KPro (S-KPro), the Pintucci Biointegrable keratoprosthesis, the

supraDescemetic synthetic cornea, the Moscow Eye Microsurgery Complex keratoprosthesis (MICOF), and several others (Gomaa et al. 2010).

Outcome

Keratoprosthesis surgery has varying success depending on a number of factors including the type of keratoprosthesis and indication for which it was used. With OOKP, one study showed that 53% of patients had better than 20/200 vision at 5 years. For BKPro, another study showed that 56% of patients had better than 20/200 vision at 1 year. With regard to retention of the keratoprosthesis, for the OOKP, studies show the probability of retention at 18 years was 85%; for the BKPro, 61% at 2 years; and for the AlphaCor (TM), retention rates at 2 years were 62% (Li et al. 2013).

Complications

Keratoprostheses increase the risk of endophthalmitis. Implantation procedures may be complicated by expulsive or choroidal hemorrhage and retinal detachment due to their open-sky nature. Other significant complications of these devices include increased intraocular pressures and glaucoma, the management of which is challenging because it is difficult to accurately assess intraocular pressure in the presence of these devices. Implant extrusion or rejection is also a risk. Complications specific to the different types of keratoprostheses include injury to the maxillary sinus or facial and jaw bones and the mucous membrane graft ulceration with OOKP, retroprosthetic membranes or persistent epithelial defects with BKPro and corneal stromal melts (both of the anterior lamella and the corneal bed), closure of the posterior lamellar opening, and opacities in the optic portion of the device with AlphaCor(TM) (Gomaa et al. 2010; Fahd et al. 2013; Li et al. 2013).

Cross-References

- ▶ Dry Eye: Definition
- ▶ Stromal Graft Rejection
- ▶ Transplantation

References

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Kestenbaum's

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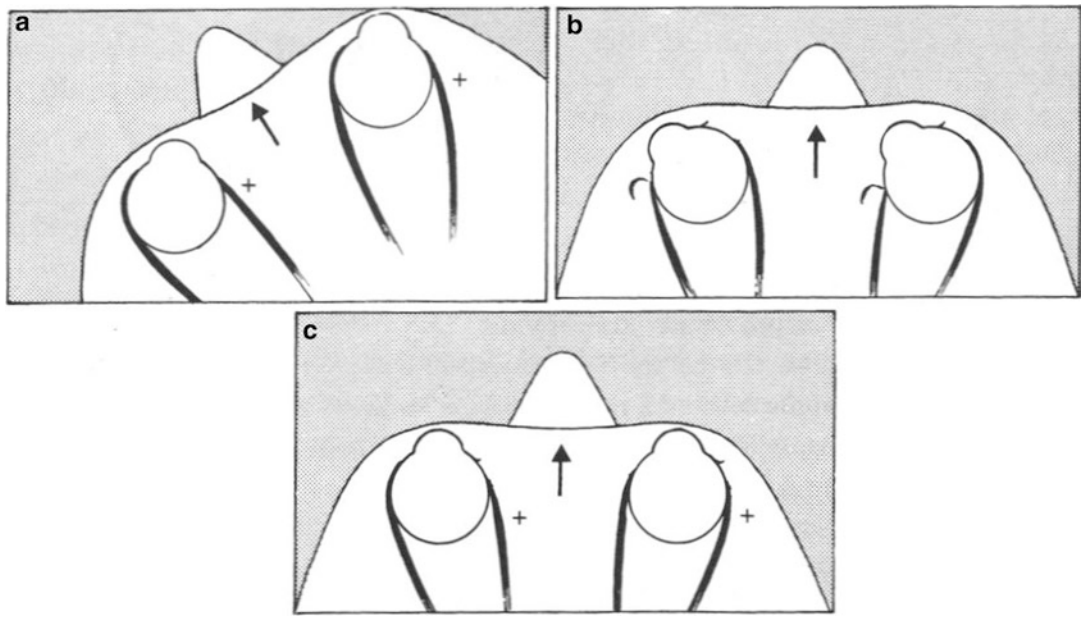
Definition

Surgery, surgical method for nystagmus-related head turn. Some patients with nystagmus rotate their head in an extreme forced posture because nystagmus is reduced due to mechanical reasons. For this group of patients, Alfred Kestenbaum (1890–1961) recommended a surgical method for a back parallel shift of those straight extraocular muscles which are contracted in this position and a resection for those straight extraocular muscles which are stretched in this position.



Kestenbaum's, Fig. 1 Kestenbaum's operation

The purpose of this rearrangement is to achieve postoperative the same innervation relation like before in the forced head turn position. It is a translator movement of neutral zone into the straight ahead view.

Kestenbaum's Operation:

(a) Preoperative both eyes are turned right. The head is rotated left. In this head forced posture, the left m. rectus medialis and the right m. rectus lateralis are innervated.
(b) Through both sides ensued combined operation, both eyes are brought into left direction.
(c) The left musculus rectus medialis and the right musculus rectus lateralis are innervated to turn the eyes into primary position. This innervation existed preoperative with forced posture head turn and was related with minimal nystagmus. This innervation exists now for straight ahead view and obviates the need of head rotation. The innervation pattern of maximal nystagmus calm is displaced into another viewing direction (Fig. 1).

Cross-References

► Nystagmus

Further Reading

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Ketorolac Tromethamine

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Synonyms

Drops: Acular, Acular PF, Acuvail, Acular LS; Tablets: Ketorolac Tromethamine 10 mg

Definition

Ketorolac tromethamine belongs chemically to the family of heterocyclic acetic acid derivatives in the pyrrolo-pyrrole group of nonsteroidal anti-inflammatory drugs. The active material blocks prostaglandin biosynthesis from arachidonic acid by irreversibly binding to both the cyclooxygenase 1 and 2 enzymes. It is used for pain relief and for treating ocular inflammation. For ocular indications, the drug is mainly used as eye drops and less frequently in tablet form (Drugs.com; Brunton et al. 2011).

Ocular Indications (Donnenfeld et al. 2006; American Academy of Ophthalmology 2014–2015a; American Academy of Ophthalmology 2014–2015b; American Academy of Ophthalmology 2014–2015c)

Ketorolac tromethamine drops are used for treating postoperative inflammation (anterior segment and cystoid macular edema) and allergic conjunctivitis. In the case of allergic conjunctivitis, it reduces conjunctival inflammation, ocular itching, and tearing, but does not have a decongestant effect and does not relieve redness. Ocular conditions that are considered potential indications for Ketorolac treatment include:

Topical (Eye Drops)

- Aphakic/pseudophakic cystoid macular edema (CME). Its effectiveness in treating uveitic CME has not been proven.
- Allergic conjunctivitis.
- Anterior segment inflammation (anterior uveitis).
- Postrefractive surgery pain.
- Given before cataract surgery to reduce intraoperative prostaglandin-induced miosis.
- Contact lens assisted pharmacologically induced keratosteepening (CLAPIKS). A pharmacological method of treating overhyperopic results after refractive surgery.

Topical/Oral

- Episcleritis.
- Scleritis: For nonnecrotizing mild diffuse disease. Nodular or necrotizing disease usually requires more potent drugs.

Contraindications (Drugs.com)

Topical/Oral

- Hypersensitivity to Ketorolac and other NSAID's.
- Asthma patients known to have aspirin-induced asthma.

Topical

- Patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface diseases, rheumatoid arthritis, or repeat ocular surgeries within a short period of time may be at increased risk of corneal adverse reactions such as corneal erosion, corneal thinning, and corneal perforation.
- Children <3 years old: Safety not established.

Oral

- Gastrointestinal disease history: active peptic ulcer disease, recent gastrointestinal bleeding or perforation, history of peptic ulcer disease, or gastrointestinal bleeding
- Renal insufficiency or risk of hypovolemic renal insufficiency
- Patients judged to have a high bleeding risk (inhibits platelet activation)
- Concomitant use with aspirin or other NSAIDs
- Obstetrics: May adversely affect fetal circulation and inhibit uterine contractions. The drug is considered Category C in pregnancy and Category D if used in the third trimester (starting at 30 week gestation). Contraindicated in late pregnancy as it may cause premature closure of the ductus arteriosus
- Breastfeeding: Oral use contraindicated while breast-feeding (excreted in breast milk). Ophthalmic solutions may be used with caution.

Dosing (Drugs.com)

- Oral: 20 mg as first dose, followed by 10 mg every 4–6 h. Do not exceed 40 mg in 24 h. In patients over 65, with renal impairment, or weight < 50 kg use 10 mg as first dose.
- Drops: Have patient tilt head back and instill prescribed number of drops into affected eye (s) as ordered. Have patient close eye(s) for 2–3 min and apply light finger pressure to bridge of nose (nasolacrimal duct) for 1–2 min after instillation to prevent systemic absorption. Do not touch top of dropper bottle to eye, fingers, or other surface.

Usage (Donnenfeld et al. 2006; American Academy of Ophthalmology 2014–2015a; American Academy of Ophthalmology 2014–2015b; American Academy of Ophthalmology 2014–2015c)

- After corneal refractive surgery: for pain relief and burning/stinging 0.4% solution, one drop four times daily for up to 4 days.
- Seasonal allergic conjunctivitis: for relief of ocular itching 0.5% solution, one drop four times daily.
- After cataract extraction: instill one drop to affected eye(s) four times daily beginning 24 h after cataract surgery and continuing through the first 2 weeks of the postoperative period.
- Before cataract surgery: to prevent intraoperative miosis. 0.4% solution four times a day for 1–3 days preoperatively.

Adverse Reactions (Drugs.com)

Ophthalmic

40%: Burning/stinging after instillation.

1–10%: Iritis, ocular inflammation/irritation, conjunctival hyperemia and/or hemorrhage, increased ocular pressure, tearing/vision blurred corneal infiltrates, corneal epithelial breakdown, superficial keratitis, corneal edema, corneal erosion, corneal thinning/ulcer, corneal perforation, allergic reactions.

Oral

Cardiovascular

1–10%: Hypertension.

<1%: Arrhythmia, bradycardia, chest pain, flushing, hypotension, MI, vasculitis.

Central Nervous System

1–10%: Headache, dizziness, drowsiness.

<1%: Aseptic meningitis, coma, convulsions, psychosis.

Dermatologic

1–10%: Pruritus, rash, sweating.

<1%: Exfoliative dermatitis, Lyell syndrome, maculopapular rash, Stevens-Johnson syndrome.

Ear Nose and Throat

1–10%: Tinnitus.

Gastrointestinal

>10%: Abdominal pain, dyspepsia, nausea

1–10%: constipation/diarrhea, flatulence, GI fullness, GI ulcers (gastric/duodenal), gross bleeding/perforation, heartburn, stomatitis, vomiting

<1%: Acute pancreatitis, exacerbation of inflammatory bowel disease, ulcerative stomatitis.

Genitourinary

1–10%: Abnormal renal function

<1%: Flank pain with or without hematuria and/or azotemia, hemolytic uremic syndrome.

Hematologic-Lymphatic

1–10%: Anemia, increased bleeding time, purpura.

<1%: Agranulocytosis, aplastic anemia, hemolytic anemia, lymphadenopathy, pancytopenia, postoperative wound hemorrhage.

Hepatic

1–10%: Elevated liver enzymes.

<1%: Liver failure.

Metabolic

<1%: Hyperglycemia, hyperkalemia, hyponatremia.

Respiratory

<1%: Bronchospasm, pneumonia, respiratory depression.

Miscellaneous
<1%: Edema; angioedema, myalgia, hypersensitivity reactions (e.g., anaphylactoid reaction, anaphylaxis, laryngeal edema, tongue edema).

Drug Interactions (Drugs.com)

ACE inhibitors: increase risk of renal impairment and decrease hypotensive effect.
Alcohol, anticoagulants, corticosteroids: increased tendency for gastric erosion and bleeding.
Aminoglycosides: increase risk of acute renal failure.
Antiepileptic agents: sporadic reports of seizures.
Aspirin, NSAIDs: risk of inducing serious NSAID-related adverse effects. Concomitant use with other NSAID drugs is contraindicated.
Bisphosphonates: may increase risk of gastric ulceration.
Clopidogrel, dextrans, heparin: increase risk of bleeding.
Cyclosporine: increases risk of nephrotoxicity.
Food: Oral administration after a high fat meal may decrease the maximal drug concentration and delay the maximal therapeutic effect.
Furosemide, thiazide diuretics: may decrease diuretic response by 20%.
Lithium and methotrexate: May increase serum levels.
Nondepolarizing muscle relaxants: Case reports of apnea.
Probenecid: increases Ketorolac levels. Concurrent use is contraindicated.
Psychoactive agents: may cause hallucinations.
Quinolones: risk of CNS stimulation and seizures from quinolones may be increased. Quinolone plasma concentrations may be increased. Use with caution.
SSRIs: increase risk of GI adverse events.

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Ketorolac Tromethamine 10 mg

▶ Ketorolac Tromethamine

Keyhole Pupil

▶ Iris Coloboma

Khodadoust Line

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Synonyms

Corneal endothelial rejection line

Definition

Khodadoust line, named after Dr. Ali Asghar Khodadoust, consists of cellular infiltrates that aggregate on the endothelium as a distinct line, which may be observed during corneal allograft endothelial rejection. These inflammatory precipitates can be seen on the endothelial surface in fine precipitates, in random clumps, or in linear

form – Khodadoust line. This line tends to migrate from the peripheral corneal to the central cornea and is typically associated with stromal edema overlying the area traversed by the endothelial rejection line. This line is often considered to be the hallmark of graft rejection. Commonly, endothelial rejection is accompanied by inflammatory cells in the anterior chamber; however, the anterior chamber reaction is usually less severe than expected given the extent of keratic precipitates present. Khodadoust line is also accompanied by corneal stromal thickening and edematous epithelium as endothelial function is hampered during episodes of rejection. The symptoms seen with Khodadoust line are typical of symptoms of inflammation and corneal edema, such as redness, sensitivity to light, decreased vision, discomfort, halos around lights, and pain. Other signs associated with endothelial rejection include ciliary flush and elevated intraocular pressure.

Etiology

Khodadoust line and corneal allograft rejection is an immune-mediated inflammatory process. The rejection line is made of a linearly oriented wave of leukocytes.

Occurrence

The most common form of graft rejection is endothelial rejection, occurring in 8–37% of cases of rejection. As of year 2000, nearly 47,000 corneal transplantations were performed in the United States. The cumulative risk of having allograft rejection has been shown to be 21% at years in large-scale prospective study.

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KLAL

▶ Transplantation

Klippel-Trenaunay Syndrome

▶ Klippel-Trenaunay-Weber Syndrome

Klippel-Trenaunay-Weber Syndrome

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Synonyms

Angioosteohypertrophy syndrome; Hemangiectatic hypertrophy; Klippel-Trenaunay syndrome

Definition

Klippel-Trenaunay-Weber syndrome (KTWS) is a condition that affects the development of blood and lymphatic vessels, soft tissue, and bone.

Etiology

The cause of KTWS is unknown and the disease is sporadic. No specific gene has been associated with the disorder.

Clinical Presentation

The hallmark features of KTWS are "port-wine stains" (i.e., nevus flammeus), venous and lymphatic malformations, and abnormal overgrowth of bone and soft tissue. Vascular malformations are often apparent at birth. Ophthalmic features associated with KTWS include retinal vascular abnormalities, choroidal angiomas, hypertrophy of orbital contents, iris heterochromia, orbital varices, and glaucoma.

The "port-wine stain" is caused by swelling of capillaries near the surface of the skin. They are typically flat and can range from pale to dark maroon in color.

Venous malformations in KTWS include superficial varicose veins that can cause pain, bleeding, and thrombophlebitis and abnormal deep veins that can increase the risk of deep vein thrombosis (DVT) and subsequent pulmonary embolism. Abnormal veins may also be present in the gastrointestinal tract and urinary tract leading to rectal and urinary bleeding. Angiomas of the brainstem, cerebellum, and spinal cord have been associated with KTWS. Lymphatic malformations can be present and cause swelling, pain, tissue breakdown, cellulitis, and ulceration.

The third cardinal feature of KTWS is hypertrophy of bone and soft tissue. Most often this hypertrophy is limited to one leg and can cause pain and a feeling of heaviness. If length discrepancy between legs is large enough, patients can have problems with walking and posture.

Diagnosis

The diagnosis of KTWS is made clinically although imaging studies may assist in the diagnosis. Doppler ultrasonography can be used to evaluate deep venous structures, and magnetic resonance imaging can be used to evaluate soft tissue hypertrophy.

Differential Diagnosis

The differential diagnosis includes Sturge-Weber syndrome, Parkes Weber syndrome, Jahnke syndrome, Schirmer syndrome, Lawford syndrome, Mille syndrome, and Beckwith-Wiedemann syndrome.

Prophylaxis

There is no prophylaxis for this syndrome.

Therapy

Therapy for KTWS is generally supportive and includes compression therapy to help control venous and lymphatic insufficiency, limb elevation, and pain medication. Shoe inserts may be used to manage limb-length discrepancies. Anticoagulant therapy may be indicated to reduce the risk of DVT. Sclerotherapy can be used to eliminate damaged veins and lymphatic vessels, and laser therapy can lighten the color of port-wine stains. Surgery can be used to remove abnormal veins and occasionally to debulk abnormal tissue and correct limb-length discrepancies.

Prognosis

Patients with KTWS generally do well. Care should be taken to avoid complications such as cellulitis, ulceration, skin breakdown, and hemorrhage.

Epidemiology

KTWS is estimated to affect 1 in 100,000 people worldwide. KTWS has no predilection for gender or race.

Cross-References

▶ Port-Wine Stain (Nevus Flammeus) in Sturge-Weber Syndrome

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Knapp Streaks or Knapp Striae

▶ Angioid Streaks

Knapp's Law

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Synonyms

Aniseikonia correction rule

Definition

Knapp's law is a mathematical calculation that theorizes whether contact lenses or spectacles are best for aniseikonia. According to Knapp:

- Use contact lenses for refractive aniseikonia.
- Use spectacles for axial aniseikonia.

Physiologic and neurologic aniseikonias were not taken into account by Knapp.

Aniseikonia: If the size or shape of an object is perceived differently by the two eyes, aniseikonia exists. Aniseikonia thus means a difference in size or shape between the two monocular visual impressions. This difference is not necessarily due to different retinal images. Aniseikonia can be caused by anatomical, functional (sensory) or geometric-optical factors.

In aniseikonia of anatomical (retinal) origin, the visual elements of the two retinas are differently structured, with the result that the two eyes obtain different perceptions despite identical far point refractions (isometropia) and identical retinal images.

Functional aniseikonia is caused by the central nervous system and can be produced by, for example, fixation disparity. Optical aniseikonia is due to different retinal images in the two eyes.

Different sizes of images on the retinas of the two eyes may be caused by:

1. Different overall lengths of the two eyes despite isometropia.
2. Different magnifications through fully correcting spectacle lenses in the case of anisometropia.
3. Aphakia of the two eyes.
4. Different distances of a near object form the two eyes as a result of oblique fixation of the object.

If an aniseikonia P_{SP} (in %) measured in vision testing at the corneal vertex distance d (in cm) is positive (larger visual impression belongs to the stronger hypermetropic eye or to the weaker myopic eye), a reduction in the corneal vertex distance leads to a decrease in the aniseikonia. If we ignore the shape magnification of the corrective device, the aniseikonia P_{CT} (%) to be expected in the transition to contact lenses can be simply estimated using formula:

$$P_{CT} = P_{SP} - d \cdot \Delta F'_V$$

where $\Delta F'_V$ (in D) is the anisometropic difference. As, however, geometrical-optical considerations regarding the correction of anisometropia neglect anatomical factors (structure of the retinal elements) and physiological factors (processing of the visual stimuli in the visual cortex), exact information can only be obtained by actual measurement of the aniseikonia.

Unilateral aphakia is a special case of refractive anisometropia. Correction with a spectacle lens leads to optical aniseikonia of approximately 25% (if the other eye is emmetropic). A contact lens can reduce the difference in size between the

retinal images to a few percent (about 4%). In numerous cases this permits adequate binocular vision.

Cross-References

► Aniseikonia Correction Rule

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Koerber-Salus-Elschnig Syndrome

► Dorsal Midbrain (Parinaud) Syndrome, Convergence-Retraction Nystagmus, Eyelid Retraction

KPro

► Keratoprosthesis

Krukenberg Spindles

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Synonyms

Axenfeld-Krukenberg spindle

Definition

Vertical band of pigment deposition on the posterior corneal surface.

Etiology

German pathologist Friedrich Krukenberg first described a spindle-shaped pigmentation of the cornea in 1899, which he characterized as "bilateral congenital melanosis of the cornea" (Krukenberg 1899; Hartmann 1982). He hypothesized that the retrocorneal pigmentation was a result of abnormal involution of the pupillary membrane during fetal development. However, several decades later, Vogt and others demonstrated that retrocorneal pigmentation was acquired rather than congenital in nature (Hartmann 1982).

Pigment Liberation in the Anterior Chamber

The iris is the primary structure responsible for releasing pigment into the aqueous humor. This can occur due to anatomical predisposition, such as in primary pigment dispersion syndrome (PPDS) when a posteriorly bowed iris results in excessive iridozonular contact. Other etiologies of intraocular pigment liberation include trauma, iritis, intraocular surgery, laser iridotomy, pigmented intraocular tumors, or chaffing from intraocular implants.

Aqueous Humor Convection Current

The circulation of aqueous humor within the anterior segment of a phakic eye is thought to be driven mainly by thermal convection currents. When secreted from the ciliary epithelium in the posterior chamber, the newly produced aqueous humor has a temperature approximately equivalent to core body temperature (37 °C). The cornea is considerably cooler due to exposure to the outside environment and tear film evaporation. This creates a 1.5–2 °C temperature differential across the anterior chamber that in turn generates a thermal convection current. This convection current is thought to govern the circulatory pattern of both the aqueous humor and any pigment granules suspended within (Heys and Barocas 2002).

Recent mathematical models of the human eye support the relationship between the convective flow pattern of the anterior chamber and the pattern of pigment deposition in Krukenberg spindles. In these models, particles emanating from the iris at the pupillary border tend to spend the majority of time circulating along the vertical plane near the central cornea. These particles were also noted to only come into close proximity with the cornea near the vertical midline (Heys and Barocas 2002; Kumar and Acharya 2007).

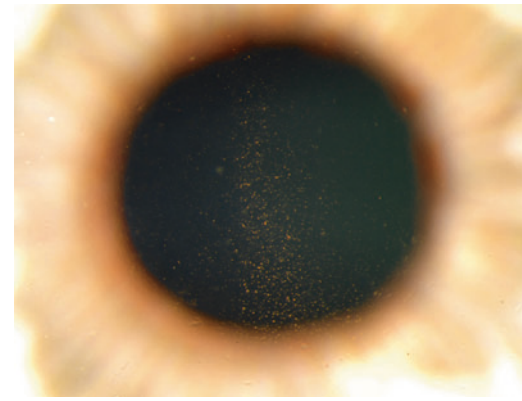
Corneal Endothelial Phagocytosis

Once pigment granules come into contact with the posterior cornea, they adhere to its irregular surface projections. Scanning electron micrograph studies have shown these surface irregularities to be comprised of microvilli, endothelial cilia, and the cellular borders between endothelial cells (Hartmann 1982). Once deposited on the surface, the pigment granules eventually undergo phagocytosis by the endothelial cells and subsequently reside intracellularly (Hartmann 1982).

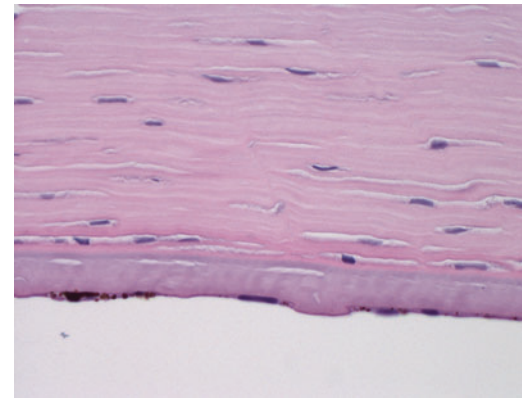
Occurrence

Endothelial pigment deposition in a Krukenberg spindle occurs in the central cornea (Fig. 1). The pigment is arranged in a vertical band measuring 0.5–2.5 mm wide and 2–6 mm in height. The pigment is most dense centrally and tapers off in a vertical fashion, thus creating a "spindle" shape (Evans et al. 1941). Due to the relatively small size and volume of the pigment granules, visual acuity is not affected by the presence of a Krukenberg spindle (Kumar and Acharya 2007).

Krukenberg spindles are classically associated with primary pigment dispersion syndrome (PPDS). However, they are not pathognomonic for this disease as Krukenberg spindles may be found in association with any condition causing pigment dispersion in the anterior chamber. Other conditions that can exhibit a Krukenberg spindle include pseudoexfoliation syndrome, trauma, uveitis, any form of secondary pigment dispersion, and eyes with a history of surgical procedures.



Krukenberg Spindles, Fig. 1 Slit lamp photograph of a Krukenberg spindle. Note the vertical band of central retrocorneal pigment deposition with tapering ends creating a spindle shape (Photo credit: Timothy J. Bennett, CRA, OCT-C, FOPS; Penn State Hershey Eye Center, Hershey, PA)



Krukenberg Spindles, Fig. 2 Hematoxylin and eosin stain of the posterior corneal surface in an eye with primary pigment dispersion syndrome. The Krukenberg spindle is visible histologically as intracellular pigment granules within the endothelial cells (Photo credit: Amy Y. Lin, MD)

Krukenberg spindles should be differentiated from senile retrocorneal pigment deposition which occurs in a diffuse pattern and is more common with increasing age (Hartmann 1982).

Histologically, Krukenberg spindles appear as granules of melanin pigment within the cytoplasm of corneal endothelial cells (Fig. 2). They may

also be seen as extracellular deposits on the posterior corneal surface.

Classification

Krukenberg spindles are an acquired form of retrocorneal pigmentation associated with intraocular pigment dispersion. Due to the association with primary pigment dispersion, the presence of a Krukenberg spindle should alert the clinician to the possibility of pigmentary glaucoma.

Cross-References

- ▶ Pigmentary Glaucoma
- ▶ Pseudoexfoliative Glaucoma
- ▶ Pseudoexfoliation Syndrome

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Kymenlaakso Syndrome

- ▶ Meretoja Syndrome

L

Labrador Keratopathy

► Keratinoid (Spheroidal) Degeneration
► Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
► Spheroidal Degeneration

Laceration

► Penetrating Eyelid Injuries

Lacerations

► Eyelid Trauma

Lacrimal Nerve

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Definition

The lacrimal nerve is the smallest of the three major branches of the ophthalmic nerve (CN V1), which in turn is the smallest of the three divisions of the trigeminal nerve (CN V). After it branches from the ophthalmic nerve, the lacrimal nerve enters the orbit through the superior orbital fissure. It follows with the lacrimal artery along the lateral rectus muscle and bifurcates just before penetrating the lacrimal gland. It then passes through the orbital septum and terminates in the skin of the lateral upper eyelid. The lacrimal nerve has only sensory function and provides sensory innervation to the lacrimal gland, conjunctiva, lateral commissure of the eye, and the skin of the lateral upper eyelids. However, before entering the lacrimal gland, the lacrimal nerve communicates with the zygomatic branch of the maxillary nerve and the parasympathetic

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fibers from the pterygopalatine ganglion that accompany it. These parasympathetic fibers provide some secretory function to the lacrimal gland.

Cross-References

► Cranial Nerve V (Trigeminal Nerve)

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Lacrimal Pump

► Rosengren-Doane Tear Pump

Lacrimal Stents

► Silicone Intubation

Lacrimal Tubes

► Silicone Intubation

Lacrimation Reflex

► Reflex Tear Arc

Lacus Lacrimalis

► Precorneal Tear Film

Lagophthalmic Keratitis

► Exposure Keratitis/Keratopathy

Lagophthalmos

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Definition

A pathological condition that results in the inability to close the eyelids.

Etiology

Lagophthalmos is a common complication associated with other diseases, such as facial nerve palsy (paralytic lagophthalmos) through loss of contraction of the orbicularis oculi muscle, the main muscle responsible for eyelid closure (Latkany et al. 2006). Further etiologies include injuries to the anterior lamella of the eyelid such as trauma, burns, or other cutaneous pathology (e.g., actinic skin damage, skin cancer) where scarring shortens the anterior lamella and does not permit proper eyelid closure (cicatricial lagophthalmos). Iatrogenic causes can also contribute to cicatricial lagophthalmos (e.g., blepharoplasty) where aggressive skin removal does not allow for proper eyelid closure. Proptosis places the individual at a greater risk for developing lagophthalmos, including tumors, thyroid eye disease, or other orbital conditions where the forward displacement of the globe and upper eyelid retraction leads to incomplete eyelid closure (Latkany et al. 2006; Bahn 2010). More recently, sunken upper eyelids and enophthalmos have been identified as causes for lagophthalmos (Latkany et al. 2006). Idiopathic causes account for a minority of the cases of nocturnal lagophthalmos (Latkany et al. 2006).

Occurrence

There are no large-scale studies demonstrating the epidemiology of lagophthalmos; however, the frequency seen within each condition is as follows (Latkany et al. 2006):

The incidence of Bell's palsy is approximately 13–28 per 100,000 individuals (Rowlands et al. 2002). Nocturnal lagophthalmos has been reported to affect every 50 out of 100,000 individuals; meanwhile, Graves' ophthalmopathy has been noted in 16 women and 3 men per 100,000 individuals (Latkany et al. 2006; Bahn 2010).

Classification

The following table lists signs and symptoms of lagophthalmos.

Sign	Symptom
Inability to completely close their eye	Dry eye
Exposure keratopathy	Complaint of foreign body sensation
Corneal scarring or thinning	Visual disturbances
Corneal perforation (rare)	Ocular pain or irritation
Conjunctival injection	Light sensitivity
Vision loss	Tearing
Increased tear film meniscus	
Increased mucous production	

Additional signs and symptoms seen with a seventh cranial nerve palsy include, but are not limited to, lower eyelid ectropion, facial hemiplegia, hearing loss, drooling, posterior auricular loss of sensation, and potential tearing associated with salivation from aberrant regeneration of the facial nerve (crocodile tears). Symptoms associated with Graves' disease include anxiety, palpitations, heat intolerance, and unintentional weight loss. Patients with ichthyosis will describe a personal and family history of dry skin, and the physical exam demonstrates dry skin.

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Lamellar Keratoplasty

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Synonyms

Anterior lamellar keratoplasty (ALK); Deep anterior lamellar keratoplasty (DALK); Descemet's membrane endothelial keratoplasty (DMEK); Descemet's stripping endothelial keratoplasty (DSEK); Endothelial keratoplasty (EK); Superficial Anterior Lamellar Keratoplasty (SALK)

Definition

Lamellar keratoplasty (LK) refers to the selective removal of diseased corneal tissue layers and replacement with healthy donor tissue. ALK techniques, such as SALK and DALK, refer to removal of the anterior corneal stromal layers while keeping intact the underlying host Descemet's membrane (DM) and corneal endothelium. EK techniques, such as DSEK and DMEK, refer to the replacement of diseased corneal endothelium and associated DM only while leaving the overlying corneal stroma intact.

Indications

Anterior lamellar transplantation techniques are an option for visual rehabilitation of corneal disease in patients whose endothelium is not

compromised. Examples include superficial stromal dystrophies and degenerations, superficial corneal scars and tumors, corneal stromal thinning (e.g., Terrien marginal degeneration, descemetocele formation, pellucid marginal degeneration), keratoconus, and certain infections (e.g., acanthamoeba), to name a few. On the other hand, EK techniques can be used in patients suffering from endothelial dysfunction without visually significant corneal stromal pathology or scarring, including Fuchs corneal dystrophy, pseudophakic bullous keratopathy, repeat corneal grafts due to endothelial cell failure, iridocorneal endothelial syndrome, and posterior polymorphous dystrophy.

Contraindications

The only absolute contraindication to ALK is endothelial dysfunction. Relative contraindications include deep scars involving DM and preexisting defects and breaks in DM (e.g., acute hydrops). For example, it may be possible to perform pre-descemetic DALK in such conditions if a moderate reduction of vision caused by focal scarring of the DM is an acceptable compromise to the replacement of largely healthy host endothelium. Additionally, depending on the comfort level of the surgeon and degree of DM involvement, defects in DM may be avoided by leaving a thin layer of the stroma in place.

Absolute contraindications to EK include visually significant corneal stromal scarring or opacity and silicone oil in the anterior chamber. There are several relative contraindications; DSEK may be able to be performed if there is adequate space in the anterior chamber with the presence of the following: glaucoma shunt device, peripheral anterior synechiae, iris abnormalities including aniridia, and anterior chamber intraocular lenses. However, DMEK is not recommended in such cases. The thin scroll of DM in DMEK can easily dislodge into the posterior chamber in aphakic and aniridic eyes or eyes with other significant iris abnormalities. In the case of a glaucoma shunt device, the donor endothelium can be damaged by mechanical trauma from the device during donor unfolding. Additionally, the thin donor tissue could potentially lodge in the lumen of the tube if there is excess pressure in the anterior chamber during unfolding.

Techniques and Principles

SALK: A lamellar flap that encompasses the corneal pathology is created and then replaced using a dissection plane of up to 160 um or approximately 30% of the anterior corneal stromal thickness. The flap is trephinated leaving a 1mm rim, and the abnormal tissue is removed. An artificial anterior chamber and microkeratome are used to create the donor disc, which is transferred to the host bed. The donor tissue may adhere spontaneously without sutures, although sutures may be necessary. More recently, femtosecond laser-assisted anterior lamellar keratoplasty (FALK) has been used to perform the lamellar dissections of both host and donor tissues in conjunction with anterior segment OCT, which may allow better matching of the thickness and diameter of the resection.

DALK: Removal of total or near-total corneal stroma in DALK can be achieved in several ways; currently, the Anwar big-bubble technique is the most popular. The cornea is suction trephined and dissected at a depth of approximately 60–80%. Air is injected paracentrally through a 27- or 30-gauge needle or specially designed cannula producing "big-bubble" separation of DM from the stroma. Entry into this space followed by removal of stromal tissue involves a process that meticulously protects and preserves DM. Donor tissue of the same size or oversized by 0.25 mm is sutured in place after donor DM is removed.

DSAEK: A 3–5 mm corneal/scleral or limbal incision is created in the recipient cornea and diseased endothelium, and Descemet's membrane is then removed under air, fluid, or viscoelastic. Lamellar dissection can be performed manually (DSEK), but some surgeons prefer automated means (DSAEK) using a microkeratome. The donor tissue is then trephined to the desired diameter (usually 8–9 mm). The trephined donor posterior lenticule is inserted into the recipient anterior chamber using forceps, glides, or specialized inserters. Once unfolded, an air bubble is used to

appose the graft to the recipient stroma. Methods to facilitate adhesion include scraping the peripheral recipient bed, using midperipheral vent incisions to drain fluid from the interface, and using a roller to sweep the corneal surface. An inferior peripheral iridotomy performed prior to donor insertion can be used to allow nearly full air fill in the anterior chamber at the end of the surgery without producing pupillary block.

DMEK: The donor graft can be prepared by using microforceps to strip DM after trephination of a corneoscleral button or done in more stepwise fashion using an intact corneoscleral rim: (a) DM is scored just inside the trabecular meshwork using a Y-hook and then freed circumferentially with a microfinger; (b) smooth forceps are used to partially peel the DM in quadrants, leaving the center attached; (c) the membrane is floated back into position and the donor trephined lightly into the stroma; and (d) DM is peeled centrally to complete the process. Following a central recipient descemetorhexis, the scrolled donor membrane is inserted using IOL injectors or a glass pipette with an attached bulb to draw up the donor and then inject it into the anterior chamber. Once in the eye, the donor is gently unfolded using techniques such as a combination of short bursts of BSS and air under the graft or using air between the donor and the recipient stroma. Once the donor is unfolded in the correct orientation, air is injected beneath the graft to appose it to the recipient cornea. While some surgeons remove part of the air after 1–2 h to avoid pupillary block, others perform an inferior iridotomy and maintain nearly complete air fill.

Outcomes

SALK/FALK: One series reported improved best corrected visual acuity (BCVA) in all nine eyes at final follow-up with BCVA $\geq$ 20/40 in seven of nine eyes within the first month. Refractive astigmatism also improved by an average of 0.7 diopters. In a series of patients who underwent FALK, 54% of all patients had BCVA greater than 20/30 at the 12-month follow-up, while in another, the mean difference between preoperative and postoperative BCVAs was a gain of 8.0 lines. Graft failure and immunologic rejection episodes are rare with SALK, and an incidence of 0% has been reported in several series.

DALK: Several studies have shown that refractive spherical equivalent, BCVA, contrast sensitivity function, and higher order aberrations in DALK are comparable to PK, especially in keratoconus patients. However, DALK has been shown to significantly reduce the risk of graft rejection and failure relative to PK given the endothelium is not transplanted. Though epithelial and stromal rejection, as well as subepithelial infiltrates can occur, these usually respond well to topical corticosteroids: all 25 patients in two combined reports who suffered from stromal rejection achieved resolution with a clear cornea with the institution of topical corticosteroid therapy.

DSEK/DSAEK: After DSEK, BCVA often ranges from 20/25 to 20/40, precluding other ocular abnormalities. Decreased postoperative visual acuity can be due to superficial irregularities, subepithelial fibrosis, or alterations of the posterior corneal curvature due to irregularities from the lamellar dissection and thickness of the donor tissue. With DSEK, in contrast to PK, there is seldom severe visual loss in an otherwise normal eye from irregular astigmatism or anisometropia. While PK induces on average, 4–5 D of cylinder, the average surgically induced astigmatism with DSEK ranges from −0.4 to +0.6 D with a median of +0.1 D. In addition, DSEK does not require a hard contact lens to achieve best vision. The 5-year graft survival rates for DSEK are reported to be similar to those for PK (95% vs. 93% for Fuchs dystrophy and 76% vs. 73% for pseudophakic or aphakic corneal edema). However, though preexisting glaucoma has been associated with poor long-term PK graft survival, eyes with preexisting glaucoma but no glaucoma surgery have been reported to have a 94% 5-year survival rate. The reported mean endothelial cell loss after PK ranges from 16% to 45% at 1 year, 29–54% at 2 years, and 70% at 5 years. With DSEK, these values range from 13% to 54% at 6 months, 15.6 to 61% at 1 year, and 53% at 5 years (single report).

DMEK: DMEK has been shown to result in visual outcomes that are superior to DSEK and achieved in shorter timeframes. For example, the

3-month rates of 20/20 and 20/25 vision with DMEK exceeded the best rates reported with DSAEK at 6 months and beyond. In one series, at 1 year, 39% of the eyes recovered 20/20 or better BCVA, 79% had 20/25 or better, and 97% could be corrected to 20/30 or better; similar results have been reported by other authors. The risk of rejection was lowest with DMEK in a recent head-to-head comparison of DMEK, DSAEK, and PK performed for the same indications and with the same steroid regimen. Only 1 of 141 DMEK grafts (0.7%) experienced a rejection episode versus 54 of 598 DSAEK grafts (9%) and 5 of 30 PK grafts (17%). The average endothelial cell loss after DMEK was 32% at 6 months (three series), 36% at 1 year (two series), and 34% and 42% at 2 and 3 years, respectively (single report). As with the early DSEK data above, these DMEK results represent early surgical techniques and learning curves in a challenging procedure, and levels of endothelial cell loss may decrease as techniques and surgeon experience improve.

Potential Complications

SALK/FALK: Complications such as residual corneal pathology, interface haze or opacification, anisometropia, recurrence of pathology, haze after adjunctive PRK, dry eye, and epithelial ingrowth have been reported.

DALK: Descemet detachment or pseudo-double anterior chambers can result from fluid in the graft-host interface from a microperforation or retained viscoelastic material. Other potential complications include inflammatory graft necrosis, opacification and vascularization of the interface, epithelial rejection, microbial infections, subepithelial infiltrates, visually significant wrinkles of DM, and stromal rejection.

DSEK/DSAEK: The most common complication is dislocation of the graft, sometimes requiring another air bubble to reattach the tissue; this has been shown in several series to be between 23% and 26%. Other potential complications include pupillary block from air fill of the anterior chamber (avoided with inferior PI), epithelial ingrowth, interface opacification, interface infection, primary graft failure, endothelial cell loss, and cystoid macular edema. Naturally, suture-related complications – some of the main complications after PK, such as infiltrates/abscess, astigmatism, and suture erosions – do not occur with EK procedures.

DMEK: In addition to the complications with DSEK/DSAEK listed above, due to the delicate scroll of graft tissue used with DMEK, the graft itself can be lost. Early studies reported high donor-tissue loss, but this is now rare with improved donor preparation techniques, including the ability of eye banks to prepare DMEK tissue.

Cross-References

▶ Deep Anterior Lamellar Keratoplasty (DALK)
▶ Deep Lamellar Endothelial Keratoplasty (DLEK)

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Langerhans Cell Histiocytosis

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Definition

Langerhans cell histiocytosis (LCH) is a rare disease involving clonal proliferation of Langerhans

cells (Cotran 2005, Halpern 1997). These abnormal Langerhans cells area derived from bone marrow and capable of migrating to either skin or lymph nodes. LCH is a part of clinical syndromes referred to as histiocytoses, which are characterized by an abnormal proliferation of histiocytes (or activated dendritic cells and macrophages). There are three classes of histiocytoses: Langerhans cell histiocytosis (Class I), non-Langerhans cell histiocytosis (Class II), and malignant histiocytosis (Class III). LCH was previously called histiocytosis X, but was renamed in 1985 (Cotran 2005, Halpern 1997, Satter 2008).

Etiology

Langerhans cells are dendritic cells containing large Birbeck granules found in the epidermis, lymph nodes, and other organs. During infection of an area of skin, Langerhans cells process microbial antigens and become fully-functional MHC class II antigen presenting cells. In LCH, these cells begin to clonally proliferate and can cause damage to skin, bone, lungs, and endocrine glands (Cotran 2005).

Classification

LCH is divided into three types: unifocal, multifocal unisystem, and multifocal multisystem (Cotran 2005).

Unifocal disease involves a slowly progressive, localized disease that may develop in bones, skin, lungs, or the stomach.

Multifocal unisystem disease is usually characterized by fever, bone lesions, and diffuse eruptions often on the scalp. It is usually seen in children. Approximately one half of patients have involvement of the pituitary stalk, causing diabetes insipidus. The triad of diabetes insipidus, exophthalmos, and lytic bone lesions is further classified as Hand-Schuller-Christian disease.

Multifocal multisystem disease involves rapid Langerhans cell proliferation in many tissues. Also known as Letterer-Siwe disease, it is usually seen in children less than 2 years of age, and survival prognosis with chemotherapy is approximately 50%. Fifty-one percent to seventy-one percent of children under age 4 present with multisystem disease, whereas 70% of adults present with disease involvement of a single organ system only (Cotran 2005, Halpern 1997).

A fourth type of LCH is pulmonary Langerhans cell histiocytosis, which occurs exclusively in cigarette smokers. Many patients experience a full recovery with smoking cessation, while others will lead to pulmonary fibrosis and pulmonary hypertension (Cotran 2005, Halpern 1997, Satter 2008).

Prevalence

LCH affects children with a peak incidence between 5 and 10 years of age. The incidence below age 10 is approximately 1/200,000 and is approximately 1/560,000 in adults. It is twice as common in males as in females and is most prevalent in Caucasians (Cotran 2005).

Clinical Features

The proliferation of Langerhans cells invokes an inflammatory response leading to fever, weight loss, and lethargy. Other symptoms depend on site of involvement.

- Skin involvement often leads to scaly, erythematous rash. Extensive rash is seen on the scalp in up to 80% of LCH patients.
- Bone involvement usually involves painful osteolytic bone swelling. The most frequently affected sites are the skull and orbit and then flat bones and long bones of the upper extremities.
- Bone marrow involvement may lead to anemia or pancytopenia.
- Lymph node involvement may lead to enlargement of lymph nodes, liver, or spleen in up to 50% of cases.
- Hypothalamic pituitary axis involvement often leads to diabetes insipidus.
- Other organ involvement leads to deficiencies of that particular organ system. Organs involved in multiorgan disease involve the spleen, liver, lungs, and intestines.

Diagnosis

LCH is confirmed by the presence of Langerhans cells on tissue biopsy. Since 50–80% of patients have skin involvement, a superficial biopsy site is usually accessible. Using light microscopy and hematoxylin-eosin stain, Langerhans cells have pink granular cytoplasm and distinct cell margins. Definitive diagnosis may be determined by the presence of Birbeck Granules on electron microscopy or CD1 positivity on immune-cytochemical stain. Initial workup should include complete blood count with differential and liver function testing (Pinkus et al. 2002). Cranial X-rays should be ordered, as should pulmonary function testing with pulmonary biopsy if a restrictive pattern is found. CT or MRI should be ordered to evaluate for osteolytic bony involvement, as well as for LCH involvement of the Sella Turcica.

Treatment

Treatment is determined by the extent of the disease and the number of organ systems involved. Next, the number of sites of disease involvement (unifocal vs. multifocal) should be determined, as well as whether organ dysfunction is present.

Solitary skin or bone lesions may be treated by excision, topical steroids, or localized radiation. Topical nitrogen mustard is also used for certain unifocal skin eruptions (Halpern 1997, Satter 2008).

Multifocal disease is treated by a combination of chemotherapy and systemic steroids (Halpern 1997, Satter 2008). High-dose, systemic prednisone is considered first-line therapy. Chemotherapy usually includes a combination of alkylating agents, vinca alkaloids, or antimetabolites based upon the LCH III treatment protocol. This protocol has numerous treatment arms based upon location of disease, organ systems involved, and whether organ dysfunction is present. Age is also factored into choosing how aggressively to treat LCH (younger patients have a worse prognosis). An effort has been made to monitor early response to chemotherapy. Patients who respond to chemotherapy have roughly a 90% survival rate, whereas survival rate in patients who do not demonstrate early response drops to 17–34%. Thus, nonresponders need to be started on a more aggressive regimen (Halpern 1997, Satter 2008).

Due to the high prevalence of Pituitary stalk involvement with orbit and/or scalp involvement, orbital lesions are treated locally and systemically with steroids and chemotherapy (Halpern 1997, Satter 2008, Harris 2006). Orbital lesions are often removed through excision, and high-dose prednisone and an appropriate chemotherapy regimen are recommended based on the threat to the central nervous system. Diabetes insipidus resulting from pituitary stalk involvement is often permanent and may need to be treated using lifelong nasal desmopressin supplement.

Prognosis

Prognosis is superb for unifocal disease. Patients who present at a younger age and those with organ dysfunction due to widely disseminated disease have the highest mortality. Lung, liver, spleen, or hematopoietic system involvement portends a worse prognosis. In general, 30% of patients with multifocal disease will achieve remission, 60% will develop chronic disease, and mortality rate is approximately 10%.

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Lanthony Tritan Album

▶ Lanthony Tritan Plates, in Color Vision Evaluation

Lanthony Tritan Plates, in Color Vision Evaluation

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Synonyms

Lanthony Tritan Album

Definition

It is a clinical test for rapid detection of blue-yellow color (tritanopic) vision defects.

Basic Characteristics

The Lanthony tritan plates consist of six pseudo-isochromatic plates numbered 0 through 5. Each plate is composed of small gray circles of different shades that together create a square. The circles in one corner of the square are colored to form a smaller square. The patient is asked to determine which corner of the larger square contains the smaller square of a different color. Plate 0 contains a smaller square that is orange and serves as a demonstration plate. Plates 1 through 5 contain violet squares that decrease in saturation progressively from plate 1–5. Thus, the difficulty of reading the plates increases from plates 1–5. The score is on scale of 5 and is determined by the number of the last plate the patient was able to read.

Lanthony tritan plates are used in the clinical setting to detect defects in blue-yellow vision. Blue-yellow vision defects are most often acquired secondary to conditions such as macular disease, optic atrophy, and glaucoma. Defects in red-green vision are not assessed with these plates.

Cross-References

▶ Contrast Sensitivity

Further Reading

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Laser Focal Treatment

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Synonyms

Photocoagulation

Definition

Ophthalmologists have been using lasers to treat ophthalmic disease since the early 1960s. LASER is an acronym for light amplification by stimulated emission of radiation. There are many types of lasers and most are named for the active medium that they employ to amplify light energy. For example, an argon laser uses ionized argon gas as the active medium. Other examples of active media are rhodamine, carbon dioxide, ruby, Nd:YAG, krypton, and semiconductor materials (termed diode laser). When energy is introduced to the active medium, it is amplified by the excitation of atoms within the medium. The amplified light energy is then emitted as laser energy at a specific wavelength.

Regarding the treatment of ophthalmic diseases, laser energy is used to induce photocoagulation, photodisruption, or photoablation of targeted ocular tissues. We will limit our discussion to the photocoagulative effects of focal laser therapy. When laser energy is absorbed by retinal pigments (melanin, xanthophyll, hemoglobin) and converted to thermal energy, the subsequent temperature rise in the targeted tissue and causes denaturation of tissue proteins and coagulative necrosis.

Indication

While there are many indications for focal laser treatment in ophthalmic diseases, common indications include macular edema due to diabetes or branch retinal vein occlusion and retinal tears/holes requiring retinopexy. Less common indications include choroidal neovascularization (CNV), Coats' disease, arterial macroaneurysm, and retinal hemangioma.

The microvascular insults (e.g., microaneurysms) induced by diabetic retinopathy and/or branch retinal vein occlusion often result in macular edema and decreased visual acuity. Focal laser treatment aims to seal these microvascular insults and decrease the associated macular edema. The Early Treatment Diabetic Retinopathy Study (ETDRS) concluded that all diabetic patients with clinically significant macular edema should receive focal laser treatment.

Due to advances in pharmacological therapy, however, focal laser treatment is less commonly employed for center-involved macular edema associated with diabetes or branch retinal vein occlusion. Nevertheless, it remains as a good therapeutic option in cases with suboptimal response to pharmacological intervention. Similarly, focal laser treatment was previously the primary treatment for CNV; however, it is rarely used currently due to advances in pharmacological therapy for subfoveal CNV.

The goal of prophylactic laser treatment for retinal breaks is to create a chorioretinal scar around the break and prevent fluid from accumulating in the subretinal space. Not all retinal breaks require prophylactic laser retinopexy and there exists a large literature regarding barrier recommendations for the many types of retinal breaks. Examples of retinal breaks include horseshoe tears, retinal dialyses, operculated tears, and atrophic holes. Areas of peripheral retinal degeneration may also be treated with prophylactic laser retinopexy.

Contraindication

None

Techniques and Principles

Focal laser treatment is most often delivered at the slit lamp with the surgeon controlling laser exposure time, power, and spot size. Topical anesthesia is usually employed to facilitate laser treatment, and peribulbar or retrobulbar anesthesia, while rare, may also be used. A contact lens is commonly employed, and surgeons must be careful to understand the orientation (inverted vs upright) of the image as any disorientation during treatment could lead to accidental burns of important retinal anatomy. The surgeon must also be aware of the magnifying effects that the contact lens may have on laser spot size.

When working in sensitive areas such as the macula, the surgeon must optimize laser

parameters to minimize unnecessary damage to adjacent retinal tissue. Examples of laser parameters for focal laser treatment of diabetic macular edema are laser exposure time 0.1 s, laser power 50 mW, and laser spot size 50–100 μm. The surgeon must titrate these settings with the goal of achieving a light retinal burn, evidenced by slight blanching of the targeted retinal tissues.

The choice of optimal wavelength must also be made. The wavelength and absorption characteristics of green and yellow lasers make them useful in treating retinal vascular disease and other ophthalmic conditions. Red laser, with its longer wavelength, can be used to penetrate nuclear sclerotic cataracts, but it causes deeper burns with a higher level of patient discomfort. Conversely, energy from blue lasers is easily scattered by ocular tissues due to its shorter wavelength.

Micropulse photocoagulation involves a series of short laser pulses (approximately 200 μs) separated by a longer rest interval (approximately 1,800 μs). The rest interval allows for heat dissipation and decreased damage to adjacent delicate retinal tissues. Micropulse therapy is often used in a subthreshold manner meaning that no visible intraretinal damage is visible during or after treatment. The goal of subthreshold micropulse laser photocoagulation is to provide treatment while avoiding damage to sensitive photoreceptor cells.

Outcome

ETDRS concluded that focal laser treatment for clinically significant macular edema in diabetes decreased the risk of moderate vision loss by 50%. The Branch Vein Occlusion Study showed that focal laser treatment for macular edema secondary to branch vein occlusion improved vision compared to observation (65% of treatment group gained $\geq$2 lines of vision compared to 37% of observation group).

Advancements in pharmacological therapy for center-involved macular edema have led to a decrease in focal laser treatment; nevertheless, it remains as a good therapeutic option in cases with incomplete response to pharmacological intervention.

Complications

The complications of focal laser treatment are caused by excessive energy use or misdirected laser energy. Corneal, iris, and lenticular burns are possible. Chorioretinal complications of focal laser treatment include foveal/foveolar burns, transient increase of edema, Bruch membrane ruptures, choroidal neovascularization, and subretinal fibrosis. Damage to the optic nerve may also occur.

Cross-References

- ▶ Central Retinal Artery Occlusion, Ocular Ischemic Syndrome
- ▶ Clinically Significant Macular Edema (CSME)
- ▶ Diabetic Macular Edema
- ▶ Diabetic Retinopathy

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Laser In Situ Keratomileusis

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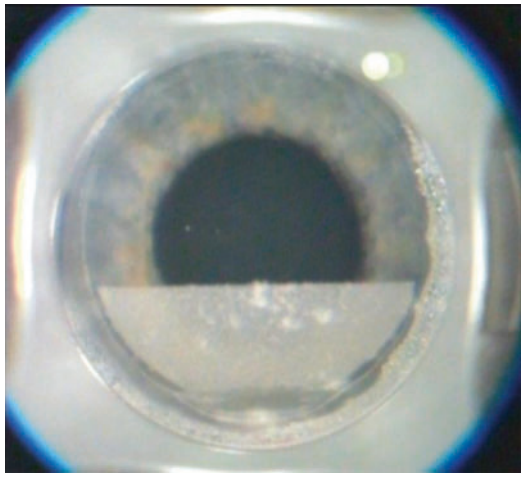
Definition

The ablation of stromal corneal tissue to modify corneal curvature and thus the ocular dioptric



Laser In Situ Keratomileusis, Fig. 1 Flap cut with a femtosecond laser. Shown is the intrastromal lamellar cut at 100 μm depths (Intralase FS60, Abbot)

power to correct ametropia by an excimer laser after cutting and opening of an anterior corneal lamella (flap) is called laser in situ keratomileusis (LASIK) (Kohnen et al. 2008; Fig. 1).

Basic Characteristics

History

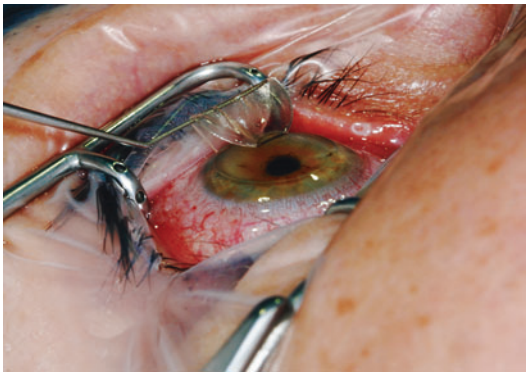
Already in 1980, *Barraquer* introduced a method of lamellar corneal surgery to correct ametropia. His "Keratomileusis In Situ" was basically the mechanical cutting of two central corneal lamellae. The first to open the corneal stroma was not a complete cut but already a flap with a hinge. The second was a complete mechanical keratectomy to change the corneal curvature. However, the flap had to be sutured after the surgery, and the precision of this method was poor. It was in 1990 when *Pallikaris* came up with the idea to combine *Barraquer's* method with the recently developed photorefractive keratectomy (PRK). *Seiler*, *McDonald*, and others proved shortly before that excimer lasers are capable of corneal tissue ablation with μm-precision. Thus, *Pallikaris* could use them to replace *Barraquer's* second total mechanical keratectomy, resulting in precise tissue ablation and thus less complications and better visual results. Since then, the precision of laser systems, ablation profiles, the knowledge of surgical problems, and physiological optics have increased a lot. The mechanical flap cut is at the moment being more and more replaced by more precise femtosecond laser flaps.

Tests/Diagnostics

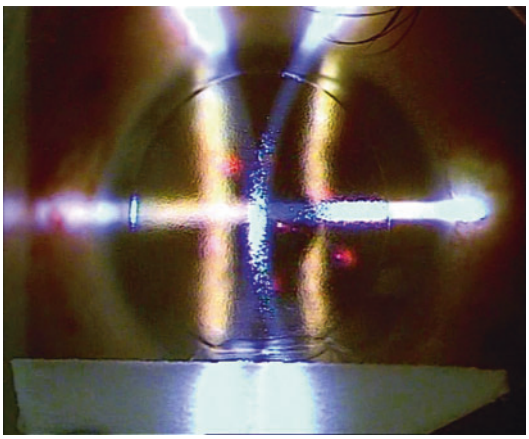
Important preoperative diagnostics to evaluate a patient's eligibility for LASIK and to plan the surgery include manifest refraction, uncorrected and best-corrected visual acuity, pachymetry (optical or ultrasound), corneal topography (Placido) and/or tomography (Scheimpflug), infrared pupillometry for the evaluation of mesopic pupil size, an anamnesis of prior ocular surgery, as well as an ophthalmic inspection to exclude retinal pathology, or blurred intraocular media. Also the patient's expectations and visual requirements need to be taken into consideration. From all these measurements, the decision pro- or contra-LASIK has to be made. Several guidelines exist worldwide, concerning treatment planning, range of possible corrections, and inclusion and exclusion criteria (e.g., by the German Ophthalmological Society and the Professional Association of German Ophthalmologists, Kohnen et al. 2011). These indicate a safe application of LASIK for myopia correction from −1D to −8D (in exceptional cases up to −10D), for hyperopia correction from +1D to +3D (in exceptional cases up to +4D), and astigmatism up to 5D, always considering the absolute refractive power in the strongest meridian, not the spherical equivalent (SE) (Kohnen et al. 2011).

Procedure

The LASIK procedure starts usually with marking of the 0–180° axis after administration of topical anesthesia to avoid intraoperative torsional malpositioning. In case of a cyclotorsional eyetracker, this step can be avoided. Then the patient is placed in a supine position, and the flap cut is being performed, either with a mechanical microkeratome or a femtosecond laser (Fig. 1). This is followed by the opening of the flap with a spatula (Fig. 2), centration of the excimer laser, excimer laser ablation (Fig. 3), and repositioning of the flap including rinsing of the interface. A contact lens can be placed



Laser In Situ Keratomileusis, Fig. 2 LASIK flap in vivo while being opened with a spatula (Geuder)



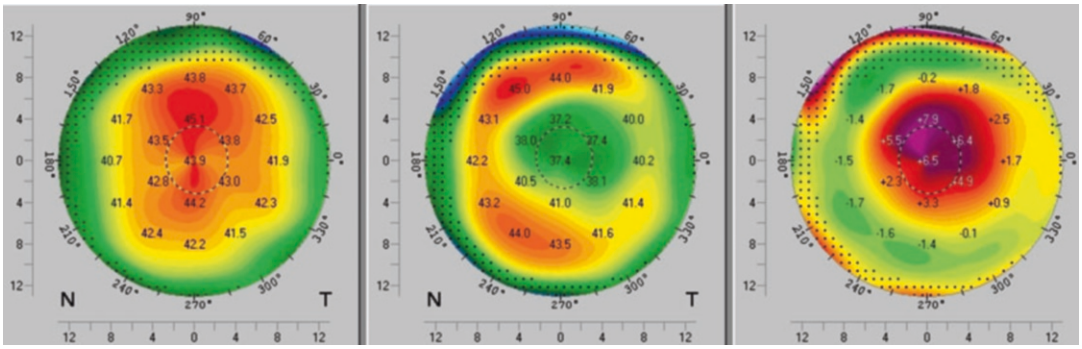
Laser In Situ Keratomileusis, Fig. 3 Excimer laser application in vivo (AMARIS, Schwind)

to protect the cornea for the first 24 postoperative hours. Postoperative medication includes steroids and artificial tears (Kohnen et al. 2008; Fig. 4).

Results

A meta-analysis by *Sakimoto* and colleagues (2006) summarizes the results of different prospective trials on (among others) LASIK. They show that the procedure is precise up to approximately -7D of myopia correction. The percentage of patients within 0.5D of SE is approximately 80%, 3–6 months after surgery. When the treated SE is higher, between -7D and -12D, the rate is only about 60–70%. In case of hyperopia, the threshold lies between 2D and 4D. These results match with the guidelines mentioned above (Kohnen et al. 2011). Another exemplary trial by Rosman and coworkers (Rosman et al. 2010) shows 10-year results of a LASIK cohort. The inclusion criteria were much less restrictive in this trial than they are today. Mean treated SE here was −14.33D. 67% of eyes were within +/−1.00D of emmetropia at 2 years after surgery, compared to 42% at 10 years. Percentages of patients within 0.5D of SE using today's ablation techniques are about 85% in 6–12 months follow-up trials (Kohnen et al. 2008).

According to another meta-analysis (Solomon et al. 2009), comparing different elective surgical



Laser In Situ Keratomileusis, Fig. 4 Corneal topography (anterior axial curvature map [D] pre- (*left*) and post (*middle*) LASIK, as well as the differential map, indicating the change in corneal curvature induced by the LASIK procedure (*right*)). Shown is an aspheric LASIK to correct compound myopic astigmatism (Pentacam HR, Oculus)

procedures, the rate of patient satisfaction after LASIK is 95%, the highest documented rate of all evaluated procedures.

However, there are certain risks and typical complications. These include incomplete or irregular flap cuts (being mainly a problem of mechanical keratomes), over- and undercorrection (which can usually be solved by retreatment), and others like diffuse lamellar keratitis, haze infections, or scars. Nearly all patients suffer from postoperative dry eye, as the flap cut also cuts the corneal nerves resulting in decreased corneal surface sensitivity and less tear film production. The problem usually solves at 1–3 months postoperatively without any therapy. Artificial tears may however be administered. The worst case scenario is the iatrogenic ectasia, a weakening of the cornea; manifestation and therapy are comparable to keratoconus, either by too much tissue ablation or by applying the LASIK procedure to an already weak cornea, e.g., in subclinical forme fruste keratoconus.

Cross-References

- ▶ Ametropia: Definition
- ▶ Astigmatism
- ▶ Choroidal Neovascularization: Myopia
- ▶ Hyperopia
- ▶ Iatrogenic Ectasia
- ▶ Lamellar Keratoplasty
- ▶ Photorefractive Keratectomy (PRK)
- ▶ Spherical Equivalent

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Laser Iridotomy

▶ Iridotomy

Laser Ray Tracing

▶ Ray Tracing

Laser Speckle

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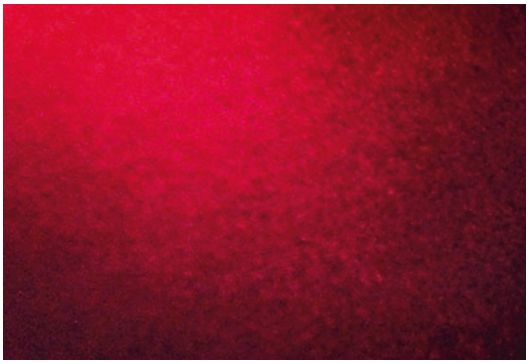
Introduction

Speckle pattern is a highly granular and contrasted intensity pattern that is observed when a coherent wave is scattered from a diffuse object. Since lasers are highly coherent sources of light (an electromagnetic wave), speckle pattern is observed when the laser light is scattered from a diffuse object. This speckle pattern is known as laser speckle.

Laser speckle can be easily observed with a laser pointer and a white paper. Take a laser pointer and shine it on a wall, dim the lights in the room, and bring the paper close to where the laser pointer is hitting the wall. On the paper, a granular pattern can be seen; this granular pattern is laser speckle (Fig. 1).



Laser Speckle, Fig. 1 Laser speckle pattern observed for laser light scattered from a diffuse sample

Explanation

When a monochromatic light is made incident on a diffuse surface, the scattered field at any arbitrary observation point is a superposition of the wavelets reflected from infinitesimal contributors on the incident surface. The infinitesimal contributors produce wavelets which have same wavelength but random phase. If the surface is rough enough such that the phase difference between two wavelets is greater than one wavelength, the superposition of these wavelets can produce a field which could be anything ranging from zero to the sum of all the wavelets. Note that if the observation point is changed then the relative phase shift between individual wavelets will also change, therefore the resulting field at this observation point can have a totally uncorrelated value from the first observation point. This results in the granular pattern observed in speckle where bright spots are observed at locations where the wavelets interfere constructively, dark spots where the wavelets interfere destructively, and intermediate values at locations where the interference is in between the two extremes.

Properties

Speckle pattern from any diffuse surface changes on changing the wavelength of light. This is because the phase relationship between individual wavelets is different for different wavelengths. Similarly, the phase relationship between individual wavelets can change with the angle of incidence of the laser beam. The speckle pattern therefore also changes if the laser is shined at different angles on the diffuse surface.

Speckle pattern has polarization dependence too. If a polarized laser beam is shined onto a rough surface, significant amount of depolarization of the laser beam is observed. If an analyzer is kept in front of the speckle pattern and is rotated, then the speckle pattern observed on the screen changes. This is happening because when a laser beam scatters from a rough surface the polarization of individual wavelets is modified in a random way. When we rotate the polarizer, we change the relative contribution of each wavelet to the interference pattern, thus changing the speckle pattern

Speckle Suppression

Although speckle is now being used for certain applications (see next section), in most of the cases speckle is a problem. The presence of speckle in an image adds noise and reduces the ability to resolve fine details. Speckle noise is a major limitation of coherence-based imaging modalities such as optical coherence tomography. Most of the techniques used to suppress speckle are based on generating a superposition of identically distributed but mutually uncorrelated speckle patterns to wash out the random granularity. The contrast reduction factor for these superposition approaches is proportional to the square root of the number of superposition states used. Typical approaches include spatial diversity, wavelength diversity, and polarization diversity.

Spatial Diversity: By spatially moving the illuminating laser beam or speckle producing sample, we can create mutually uncorrelated speckle patterns, which could then be superimposed to reduce speckle contrast. One approach to do this is to illuminate the speckle producing surface at different angles. Since the speckle pattern is different for different angles of incidence, the cumulative speckle pattern averages out and speckle pattern contrast is reduced. Other

approach is to move or rotate the speckle producing surface. If the detector's integration time is significantly large enough, then the superposition of speckle pattern from different parts of the sample is detected on the detector thus reducing the contrast of the speckle pattern.

Wavelength Diversity: As mentioned previously, speckle pattern changes with wavelength of incident light. This approach reduces the contrast of the speckle pattern by illuminating the sample with different wavelengths.

Polarization Diversity: Since speckle has polarization dependence, speckle is naturally reduced when unpolarized light is used. Although this approach is simple to implement, as polarization diversity is limited to just two orthogonal polarization states, maximum contrast reduction factor that can be achieved is limited to the square root of two.

Besides the hardware related techniques of speckle reduction described above, numerous methods of numerically removing the speckle during image postprocessing have also been proposed. These techniques use a statistical model to predict the properties of speckle pattern and then apply appropriate image processing filters to remove it.

Applications of Laser Speckle

For most applications, speckle pattern is a nuisance; however, speckle pattern can also function as the carrier of information. Since the speckle pattern is observed for rough samples and not for polished surfaces, it can be used as a measure of the surface roughness of the surface. In industrial applications where systems are sensitive to movements or deformations at micron scales, speckle can be used to sense these changes as slight movement of the sample can produce a change in the speckle pattern.

In the medical area, speckle has been used to measure the velocity of blood flow, the idea being that higher the velocity of blood flow higher will be the suppression of speckle. This approach is called laser speckle contrast imaging and has been utilized for tissue perfusion in capillaries of human skin tissue and cerebral blood flow mapping in rodents. Laser speckle has also been used to measure blood coagulation status in wounds. The Brownian motion of proteins in the blood changes with blood coagulation, thus changing the speckle pattern fluctuations, which can be detected and quantified. In ophthalmology, there are proposals to use these laser speckle-based techniques in measuring circulation in retinal blood vessels.

There is a lot of activity and interest in the medical research community to use these speckle-based techniques for medical applications. With its simplicity of implementation and relatively low cost, these speckle-based techniques have a potential to become a popular medical diagnostic technique in future.

Cross-References

- ▶ Circular Polarization
- ▶ Optical Coherence Tomography
- ▶ Retinal Blood Vessels

Lash Follicle, Tumors Arising in

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Synonyms

Pilomatrixoma; Trichilemmoma; Trichoadenoma; Trichoepithelioma; Trichofolliculoma; Tumors of pilar origin

Definition

Tumors affecting the eyelash follicle include trichoepithelioma, trichofolliculoma, trichilemmoma, and pilomatrixoma. All are somewhat uncommon and almost always benign.

Characteristics

Trichoepithelioma is a small, skin-colored nodule that occurs on the forehead or eyelids. Lesions may be misdiagnosed as papillomas or cutaneous horns, and larger lesions may have telangiectasias and resemble basal cell carcinoma. Surgical excision is curative.

Trichofolliculoma is a dome shaped, skin-colored nodule. It is umbilicated centrally and may have white lanugo hairs which may protrude from the lesion. Excisional biopsy is curative.

Trichilemmoma is a solitary lesion with a similar appearance as verrucae. They are composed of glycogen rich cells surrounding the hair follicle. Multiple trichilemmomas may be a sign of Cowden's disease, an autosomal dominant disorder characterized by oral and acral papules, thyroid goiters, lipomas, intestinal polyps, and fibrocystic breast disease. Cowden's disease combined with cerebellar hamartomas is known as Lhermitte-Duclos syndrome.

Pilomatrixoma is a lesion of young adults, arising on the base of hair follicles on the eyebrow or central upper eyelid. It presents as a subcutaneous purplish mass. Surgical excision is curative (Albert and Jakobiec 2008; Shields and Shields 1999).

Differential Diagnosis

Trichoepithelioma
Trichofolliculoma
Trichilemmoma
Pilomatrixoma

Management

See individual entities for further information.

Cross-References

- ▶ Pilomatrixoma
- ▶ Trichoepithelioma
- ▶ Trichofolliculoma

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Late Hereditary Endothelial Dystrophy

▶ Fuchs' Dystrophy Disease

Lateral Canthal Reconstruction

▶ Canthal Reconstruction

Lateral Canthoplasty

▶ Horizontal Eyelid Shortening

Lateral Canthotomy

▶ Canthotomy

Lateral Chromatic Aberration

▶ Chromatic Aberration: Definition

Lateral Gaze Center

▶ Horizontal Gaze Center

Lateral Geniculate Lesion

▶ Retrochiasmal Disorders

Lateral Medullary Syndrome

► Wallenberg Syndrome

Lateral Orbitotomy

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Definition

An orbitotomy allowing access to the deep orbit in both extra- and intraconal spaces lateral to the optic nerve.

Indications

To access the lateral and deep posterior orbit for biopsy, orbital decompression, foreign body removal, etc.

Contraindication

Any medical contraindication to surgery.

Techniques and Principles

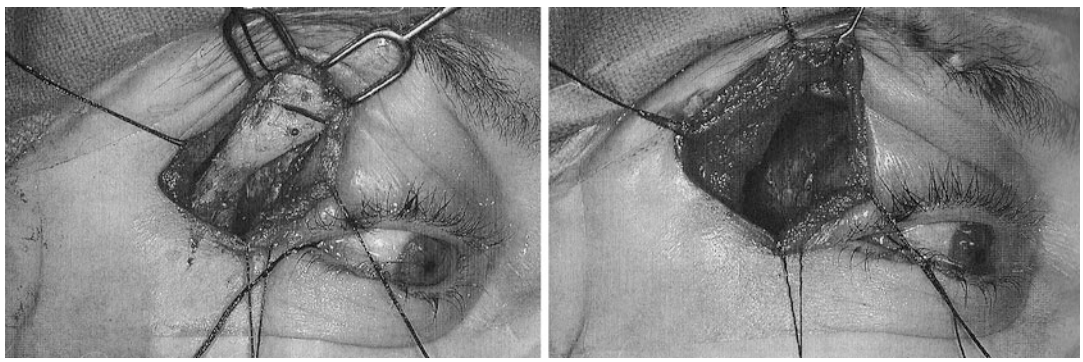
This procedure is generally performed in the operating room under sedation or general anesthesia. Often, this approach involves temporary removal of the lateral orbital rim to maximize exposure for deep lesions. A skin incision is usually placed at the lateral canthus and extended laterally as necessary, for approximately 2 cm. A superior and inferior cantholysis is performed and the lateral orbital wall is exposed. A cutting saw is used to remove the orbital rim and anterior lateral wall (Fig. 1), which is either sutured or plated back in place at the end of the case. With this technique, the surgeon has an unobstructed view into the deep lateral orbit (Cockerham et al. 2001; Nerad 2001; Levine 2003). A coronal scalp flap has also been described to access this area (Paolini et al. 2006).

Outcome

Allows for biopsy, lesion removal, foreign body removal, drainage of orbital abscess, and bony decompression as necessary.

Complications

Risks include anesthesia, bleeding, pain, infection, scarring, lower eyelid retraction, swelling,



Lateral Orbitotomy, Fig. 1 The lateral orbitotomy: Dissection has been carried down to periosteum and the lateral orbital rim has been exposed. A saw cut is shown superiorly with preplaced drill holes to replace the rim at the end of the procedure (*left*). The *right* photography reveals the view to the lateral orbit after the lateral wall segment has been temporally removed (Printed with permission from Nerad JA, ed. Oculoplastic Surgery. The requisites in ophthalmology. St. Louis: Mosby, Inc. 2001: 408)

loss of vision, damage to adjacent structures, diplopia, and need for additional procedures.

Cross-References

- ▶ Anterior Orbitotomy
- ▶ Blowout Fractures
- ▶ Coronal Scalp Flap, for Anterior Orbitotomy
- ▶ Extraperiosteal Route
- ▶ Graves Ophthalmopathy
- ▶ Orbit, Inflammation of
- ▶ Orbitotomy
- ▶ Transcutaneous Routes

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Lateral Rectus Palsy

- ▶ Sixth Nerve Palsies

Lateral Tarsal Strip

- ▶ Horizontal Eyelid Shortening

Lateral Tarsal Strip Procedure

- ▶ Tarsal Strip Procedure

Lateral Tarsotomy

- ▶ Tarsotomy

Lattice Corneal Dystrophy

- ▶ Lattice Lines

Lattice Corneal Dystrophy (LCD), Gelsolin Type (LCD2) Familial Amyloidosis, Finnish Type (FAF)

- ▶ Stromal Dystrophies

Lattice Corneal Dystrophy (LCD), Type 1

- ▶ Lattice Dystrophy

Lattice Corneal Dystrophy Type 2

- ▶ Meretoja Syndrome

Lattice Corneal Dystrophy, Gelsolin Type

- ▶ Meretoja Syndrome

Lattice Dystrophy

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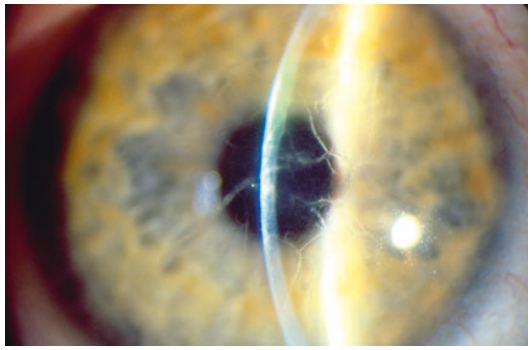
Synonyms

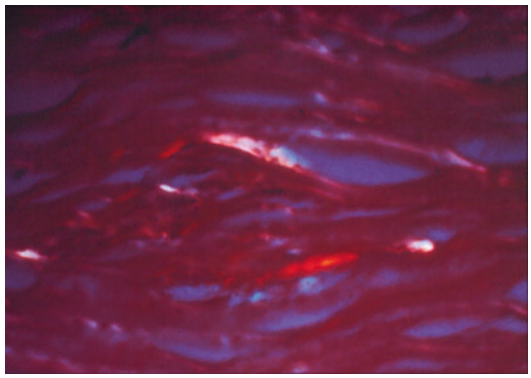
Biber-Haab-Dimmer dystrophy; Classic LCD; Lattice corneal dystrophy (LCD), type 1

Definition

There are two types of lattice dystrophy. LCD type 1 is a bilateral inherited stromal corneal



Lattice Dystrophy, Fig. 1 Central branching lattice lines with anterior stromal haze



Lattice Dystrophy, Fig. 2 Light microscopy demonstrating amyloid deposits

dystrophy involving localized corneal amyloid deposits that lead to recurrent erosion and decreased vision. There are different variants of LCD (III, IIIA, I/IIIA, and IV). Type II (Meretoja's syndrome) is a systemic amyloidosis with corneal involvement and not a true corneal dystrophy (Figs. 1 and 2) (Krachmer et al. 2011).

Etiology

LCD type 1 is autosomal dominant and caused by a genetic mutation at 5q31 gene locus. Type III variant is autosomal recessive. Type IIIA and IV variants are both autosomal dominant. LCD type II is autosomal dominant and caused by a genetic mutation on chromosome 9 (Musch et al. 2011).

Clinical Presentation

LCD type 1 presents in the first decade of life with refractile filamentary lines and anterior stromal opacities. With progression, nodules and thick threadlike spicules develop. The stroma between the lines and opacities is initially clear, but eventually, the opacities coalesce and a progressive corneal haze ensues. Like other corneal dystrophies, painful recurrent erosions and an irregular epithelial surface develop. Decreased corneal sensation and vascularization may also be present. Contrasting, type III variant has a late onset of decreased vision and is usually not accompanied with recurrent erosions (Musch et al. 2011).

LCD type II or Meretoja's syndrome presents later in life and has a systemic presentation. Cranial and peripheral neuropathies develop as abnormalities in the skin, arteries, and other organs. Eye examination reveals fewer and more peripheral filamentary lines than in LCD type I. Recurrent erosions are also more infrequent and vision is not affect until later in life than with LCD type I (Krachmer et al. 2011).

Diagnosis

On slit lamp examination, the line branch overlaps one another making a latticework pattern. In light microscopy an eosinophilic layer separates the epithelial basement membrane from Bowman's layer. This layer is made of amyloid and collagen. Amyloid deposits are also found in the stroma and stain orange red with Congo red. With a polarizing filter, the deposits exhibit green birefringence. Thioflavin T staining demonstrates fluorescence and crystal violet staining demonstrates metachromasia (Musch et al. 2011).

Transmission electron microscopy reveals extracellular masses of randomly aligned fibrils. Confocal microscopy shows linear structures in the stroma with varying reflectivity (Krachmer et al. 2011).

Differential Diagnosis

The differential diagnosis includes recurrent corneal erosion, polymorphic amyloid degeneration,

Avellino dystrophy, granular dystrophy, macular dystrophy, and prominent corneal nerves.

Prophylaxis

There is no known prophylaxis.

Therapy

Recurrent erosions are treated as needed with topical lubricants, topical cycloplegics, antibiotic ointments, bandage contact lenses, and pressure patching. If recurrent erosions are not responsive to conservative treatment, then phototherapeutic keratectomy (PTK) is an option. Lamellar and penetrating keratoplasty is reserved for when the vision deteriorates significantly. Lattice dystrophy recurs more frequently in grafts than granular or macular dystrophy (Musch et al. 2011).

Prognosis

Corneal erosions recur and persist leading to scarring and decreased vision. Visual deterioration is progressive and frequently leads to corneal transplantation in the fourth decade of life (Krachmer et al. 2011).

Epidemiology

Lattice dystrophy is rare with a 5 years prevalence rate of less than 0.001%. The onset is usually in the first decade of life and is more commonly in Caucasians. No gender predilection is noted (Weiss et al. 2008).

Cross-References

- ▶ Avellino Dystrophy
- ▶ Granular Dystrophy
- ▶ Macular Dystrophy
- ▶ Recurrent Corneal Erosion

References

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Lattice Dystrophy Type I

▶ Corneal Dystrophies

Lattice Dystrophy Type II

▶ Corneal Dystrophies

Lattice Lines

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Synonyms

Lattice corneal dystrophy; Localized corneal amyloidosis

Definition

Lattice lines are amyloid deposits in the corneal stroma, producing branching fibers that create a latticelike pattern.

Structure

Lattice lines are produced from localized corneal amyloidosis, in which amyloid is deposited in a branching pattern in the cornea. These linear deposits are generally produced from localized intracellular production of amyloid in the cornea, but may also include leakage from serum and extracellular breakdown of corneal collagen.

Amyloid demonstrates a beta-pleated fibrous protein structure, and deposits vary based on the type of amyloidosis. Amyloidosis is divided into the systemic or localized form and further classified into primary and secondary forms. In primary systemic forms of amyloidosis, amyloid deposits contain portions of immunoglobulin light chains (protein AL). In secondary systemic forms of amyloidosis, the amyloid deposits consist of non-immunoglobulin protein (protein AA), otherwise known as a degraded product of serum amyloid A protein, an acute-phase reactant protein present in the serum. In both primary and secondary amyloidosis, amyloid deposition consists of normal protein present in the serum (protein AP). In lattice dystrophy, only the protein AP is present in amyloid deposits. However, lattice corneal dystrophy type III is the exception, in which case some deposits respond weakly to antibodies for amyloid protein AA in immunohistochemical assays.

Histologically, amyloid deposits stain with Congo red, periodic Acid-Schiff, and Masson's trichrome and demonstrate dichroism and apple-green birefringence under polarized light.

Lattice lines can be seen through slit-lamp biomicroscopy, indirect illumination, and retroillumination of the eye. The refractile lines overlap one another, illustrating a latticework pattern. In early manifestations, lattice lines are seen as ovoid subepithelial opacities, anterior stromal white dots, and refractile linear lines. As lesions further progress, they can be appreciated as small nodules, or thicker, radially branching lines. With time the opacities will begin to coalesce, producing stromal haze.

All lattice corneal dystrophies (LCDs) are characterized by the presence of deposits between the epithelial basement membrane and Bowman's layer. However, multiple variants of lattice lines have been described in the different subtypes of lattice corneal dystrophies:

1. LCD1 – Numerous rodlike glassy opacities in a linear, branching pattern with more dense opacities centrally. LCD1 maintains a clear peripheral perilimbal cornea. Ultrastructural examination shows electron-dense fibrils with a diameter of 80–100 Å.
2. LCD2 – Few thick linear lines extending to the limbus.
3. LCD3 – Thick, ropy midstromal lattice lines scattered throughout the corneal stroma, which extend to the limbus.

Lattice Lines, Table 1 Lattice corneal dystrophies due to keratoepithelin gene defects

Dystrophy	Defect
Lattice I	Arg124Cys, Ala546Asp, Pro551Gln, Leu518Pro
Lattice IIIA	Pro501Thr, Arg124Thr, Ala622His, His626Ala
Lattice IV	Leu527Arg

TGFB1/BIGH3 (keratoepithelin gene) genes are responsible for corneal dystrophies inherited in an autosomal-dominant manner. Mutations in the BIGH3 gene cause amyloid deposition in different patterns. Lattice corneal dystrophy type I has an autosomal-dominant inheritance with a disease resulting in mutations at 5q31 locus. The most frequent defect is at codon 124 where the amino acid arginine is replaced by cysteine. It is proposed that common mutations at positions 124 and 555 are likely to affect protein-protein interactions, causing misfolding within the cell. Specific functions of TGFB1 in the cornea are unknown, but it may act as a cell adhesion molecule and a linker protein interconnecting matrix molecules to each other (Table 1).

Function

Lattice lines are small retractile filamentary lines composed of amyloid and contribute to corneal haze. Over time, the lattice lines will grow more

opaque and converge, contributing to central clouding and decreased visual acuity.

Clinical Relevance

Lattice lines are seen in almost all patients with lattice corneal dystrophy. Typically, lattice lines are seen bilaterally; unilateral involvement has been reported. Treatment of the disease is based on the patient's symptoms. Clinical manifestations of the disease vary based on the type of LCD a patient is diagnosed with:

1. LCD1 – Amyloid opacities commonly lead to frequent recurrent erosions and irregularity of epithelial surface, with accompanying decreased visual acuity. Central corneal sensation may also decrease. Occurs in the first decade of life.
2. LCD2 – Recurrent erosions are infrequent and visual disturbance is less than LCD1. These patients have cranial neuropathy and systemic amyloid deposition in addition to corneal amyloidosis.
3. LCD3 – Recurrent erosions are infrequent. LCD3 often occurs later in life, after 40 years of age.

Treatment for lattice lines varies based on the severity. Treatment for recurrent erosions includes patching, artificial tears, and therapeutic soft contact lenses. If visual acuity is impaired significantly, penetrating keratoplasty is the treatment of choice.

Cross-References

▶ Lattice Corneal Dystrophy
▶ Lattice Dystrophy

Further Reading

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Laurence–Moon Syndrome

▶ Bardet–Biedl Syndrome, Renal

Laurence–Moon–Bardet–Biedl Syndrome

▶ Bardet–Biedl Syndrome, Renal

Laurence–Moon–Biedl Syndrome

▶ Bardet–Biedl Syndrome, Renal

Law of Reflection: Definition

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Synonyms

Reflection law

Definition

The law of reflection refers to the reflection of light-rays off smooth conducting surfaces, such as polished metal or metal-coated glass mirrors. Consider a light-ray incident on a plane mirror, the law of reflection states that the incident ray, the reflected ray, and the normal to the surface of the mirror all lie in the same plane. The angle of reflection is equal to the angle of incidence. Both angles are measured with respect to the

normal to the mirror. The law of reflection also holds for nonplane mirrors or rough surfaces (diffuse reflection).

Cross-References

► Law of Refraction (Snell's Law)

Law of Refraction (Snell's Law)

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Synonyms

Law of Snellius; Refraction law

Definition

The law of refraction deals with propagation of light rays across a sharp interface between two transparent dielectric media. The law of refraction states that the incident ray, the refracted ray, and the normal to the interface all lie in the same plane. The angle subtend between the incident ray and the normal to the interface Θ_1 is transformed to an angle Θ_2 of the refracted ray with $n_1 \sin\Theta_1 = n_2 \sin\Theta_2$, where $n_{1/2}$ refers to the refractive indices of the media before/after passing the interface.

Cross-References

► Law of Reflection: Definition

Law of Snellius

► Law of Refraction (Snell's Law)

Le Fort Fractures

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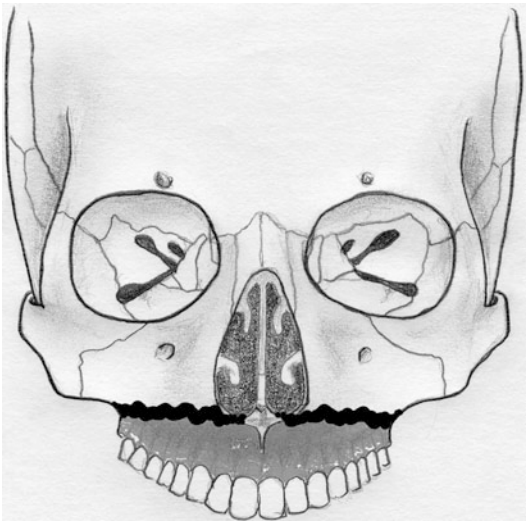
Synonyms

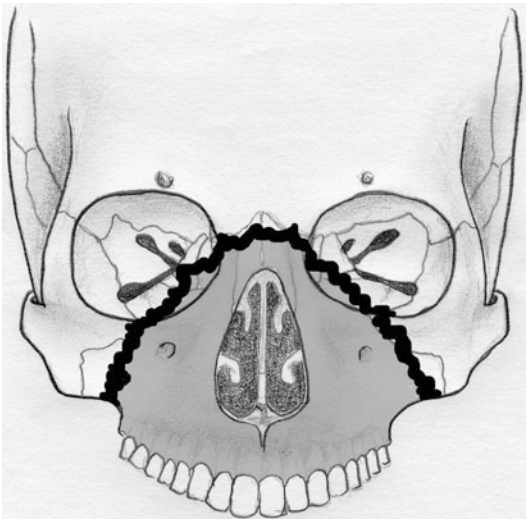
Craniofacial disjunction (Le Fort III); Guerin fracture (Le Fort I); Horizontal fracture (Le Fort I); Maxillary fractures; Pyramidal fracture (Le Fort II)

Definition

In 1901, Rene Le Fort categorized fracture patterns of the Maxilla resulting from a single blow to cadaveric skulls. The fracture lines, or "linea minoros resistentiae," described by Le Fort in 1901 are the basis for the modern Le Fort classification. A Le Fort I fracture (also known as a Guerin fracture or horizontal fracture) is a single horizontal fracture through the maxilla that passes through the septum medially, extending laterally through the pyriform rims, passing below the zygomaticomaxillary suture line, and transecting the pterygomaxillary junction to interrupt the pterygoid plates. Le Fort I fractures result in a mobile hard palate. A Le Fort II fracture (pyramidal fracture) passes through the nasal bridge medially (at or around the nasofrontal suture), extending laterally through the frontal process of the maxilla, lacrimal bones, orbital floor, inferior orbital rim, anterior wall of the maxillary sinus, passing below the zygoma, and transecting the pterygomaxillary junction to interrupt the pterygoid plates. Le fort II fractures result in a pyramid-shaped mobile bone fragment that includes the nasal complex and entire maxilla, including the

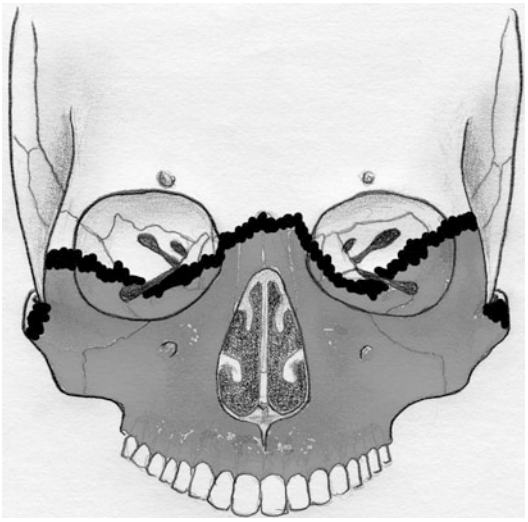


Le Fort Fractures, Fig. 1 Le Fort I fracture (Guerin fracture or horizontal fracture). The *shaded area* represents the resultant mobile bone fragment



Le Fort Fractures, Fig. 2 Le Fort II fracture (pyramidal fracture). The *shaded area* represents the resultant mobile bone fragment

hard palate. A Le Fort III fracture (craniofacial disjunction) passes through the nasal bridge medially (at or around the nasofrontal suture), extending laterally through the medial orbital rim, medial orbital wall, nasolacrimal groove, ethmoid bones, floor of the orbit, inferior orbital fissure, lateral orbital wall, zygomaticofrontal suture, and zygomatic arch. Internally, the fracture extends though the perpendicular plate of the ethmoid, vomer, and pterygoid plate interface, to the base of the sphenoid posteriorly. A Le Fort III fracture separates the entire midface from the cranium. The resultant mobile bone fragment includes the nasal complex, inferior half of the orbit, zygoma, and entire maxilla, including the hard palate. It is important to realize that pure Le Fort fractures are uncommon in clinical practice and most midfacial fractures are an amalgam of various types of Le Fort fractures. Pure Le Fort fractures occur in less than 50% of midfacial fractures (Figs. 1, 2, and 3).



Le Fort Fractures, Fig. 3 Le Fort III fracture (craniofacial disjunction). The *shaded area* represents the resultant mobile bone fragment

Basic Characteristics

Etiology

Le Fort fractures are generally the result of blunt-force trauma to the midface. Common causes include motor vehicle accidents, interpersonal altercations, assaults, falls, and sports-related injuries.

Clinical Presentation

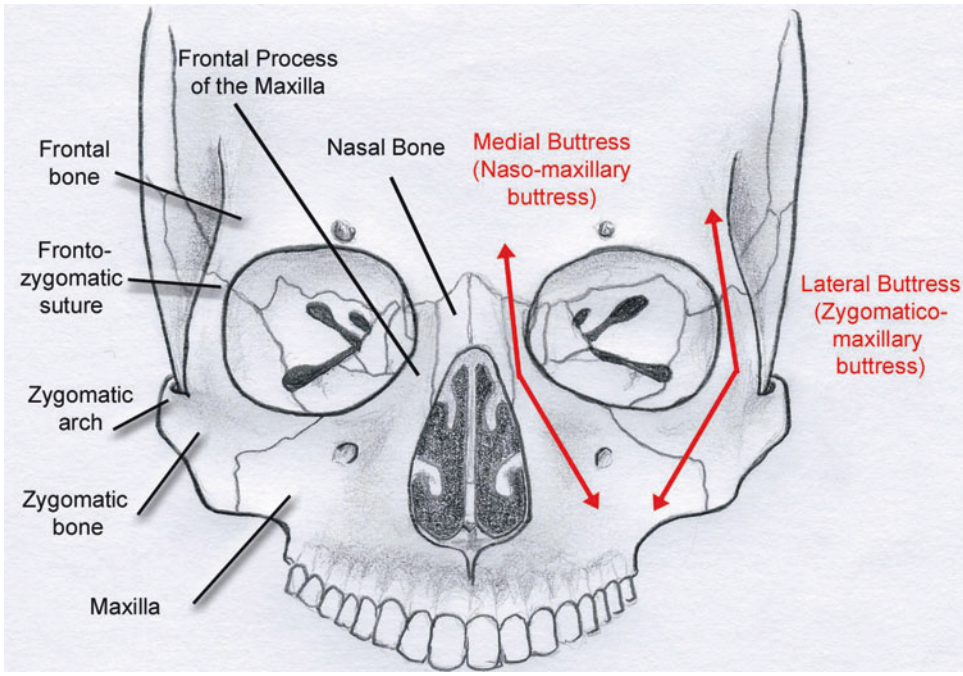
Maxillary fractures often occur as the result of significant trauma, and evaluation should

begin with airway control and hemodynamic stabilization. Serious intracranial injury may be seen in up to 38% of patients with midfacial fractures; serious ophthalmologic injury may be seen in up to 28% of patients. Spinal cord injury should be ruled out, and any overt globe injury should be evaluated. A thorough history and physical, including a complete head and neck exam, may then be performed.

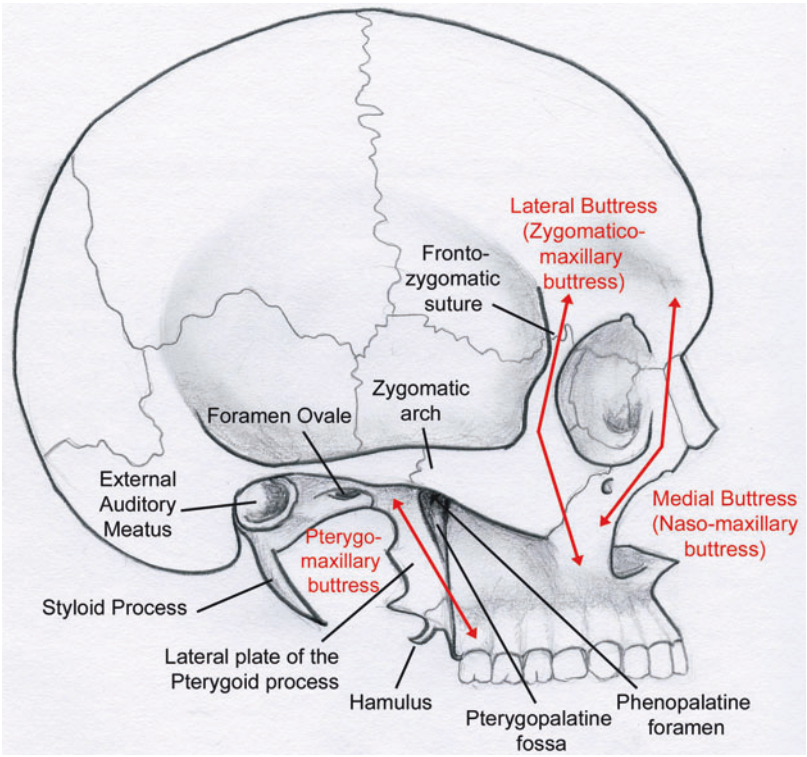
The midface is attached to the cranium by three vertical buttresses that help distribute masticatory forces and stabilize the midface: the medial buttress (frontomaxillary buttress) and lateral buttress (zygomaticomaxillary buttress) anteriorly and the pterygomaxillary buttress posteriorly. Le Fort fractures disrupt these buttresses, resulting in altered vertical height of the midface, malocclusion with open bite, and mobile bone fragments that may cause airway compromise. Mobile bone fragments that result from Le Fort fractures tend to be driven posteroinferiorly along the slope of the skull base, producing a flattened facial appearance. Palatal fractures may occur along with Le Fort fractures and intraoral ecchymosis, lacerations or palpable step-offs may be appreciated. As Le Fort II and III fractures necessarily disrupt the nasal bridge, naso-orbital-ethmoid complex, and orbital rims, these types of fractures result in more obvious external findings such as nasal deformity, subconjunctival and periorbital ecchymosis and edema, infraorbital anesthesia from injury to the infraorbital nerve, possible gaze restriction or diplopia from soft tissue entrapment, or CSF rhinorrhea from disruption of the cribriform plate. Le Fort III fractures may result in bleeding from basilar skull fractures near the stylomastoid foramen. This bleeding may track superficially, resulting in ecchymosis overlying the mastoid process and occiput (Battle's sign). Significant facial edema is common with Le Fort fractures, and it is important to keep in mind that presence of a Le Fort fracture does not rule out presence of additional maxillofacial injuries (Figs. 4 and 5).

Diagnostics

Le Fort II and III fractures involve orbital wall fractures, and the eye must be completely



Le Fort Fractures, Fig. 4 Anteroposterior view of the vertical buttresses of the facial skeleton



Le Fort Fractures, Fig. 5 Lateral view of the vertical buttresses of the facial skeleton

evaluated. Intracranial injury must also be ruled out, and suspicion for CSF rhinorrhea should be high. Maxillofacial CT scan is considered the modality of choice for diagnosis of Le Fort fractures.

Treatment

Treatment of ocular and CNS injuries should precede treatment of Le Fort fracture in the presence of a stable airway. Proper repair of complex midfacial fractures may require a surgical airway. Treatment greatly depends on the extent of the injuries and often requires a multispecialty approach.

Reconstruction of the zygomaticomaxillary buttress (lateral buttress) and fronto-zygomatic buttress (medial buttress) is an important part of restoring normal occlusion and vertical height of the midface and stabilizing the midfacial skeleton against masticatory forces. Palatal fractures may accompany Le Fort fractures, and it is important to recognize when palatal fractures are present, as palatal splints will be required during repair.

Cross-References

- ▶ Guerin (Maxillary) Fracture
- ▶ Naso-Orbital-Ethmoid Fractures
- ▶ Orbit, Inflammation of
- ▶ Orbital Floor Fracture
- ▶ Zygomatic Bone
- ▶ Zygomatic-Maxillary Complex Fractures

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Le Fort I Fracture

- ▶ Guerin (Maxillary) Fracture

Leber Hereditary Optic Neuropathy

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Synonyms

Leber optic atrophy; LHON

Definition

Leber hereditary optic neuropathy is an inherited disease that causes degeneration of retinal ganglion cells and bilateral visual loss.

Etiology

LHON is caused by mitochondrial DNA mutations and is maternally inherited. The most frequent disease causing mutation is a single base pair mutation at position 11778. Mutations at positions 3460 and 14484 are the next most common mutations. These mitochondrial mutations lead to impaired mitochondrial adenosine triphosphate production, which affects highly energy-dependent cells such as the retinal ganglion cells and leads to degeneration of the optic nerve and visual loss. Not everyone harboring one of these mitochondrial mutations will develop the disease. It is estimated that up to 50% of males and 85% of females that have a mutations will develop no signs or symptoms of the disease. This variable penetrance and expressivity can make a positive family history hard to elicit. In addition, the mutation may arise de novo.

Clinical Presentation

LHON typically affects males at age 10–30 years but both men and women can be affected. The age of onset is also highly variable. The most common presenting feature in LHON is painless vision loss OU. At onset, the vision loss is most often unilateral and associated with relative afferent pupillary defect (RAPD), but then becomes bilateral eventually. Fundoscopic examination may be normal at onset but classically reveals peripapillary telangiectasia, tortuosity of the medium-sized retinal arterioles, and "pseudoedema" of the optic disc. Pseudoedema is characterized by hyperemia and elevation of the optic disc and thickening of the peripapillary retina, without the leakage on fluorescein angiography. After visual loss the optic disc eventually becomes atrophic. The visual field defect is characterized by central or cecocentral scotomas. Occasionally, some patients may develop cardiac conduction abnormalities or other mild neurologic deficits and further evaluation is warranted.

Diagnosis

The diagnosis is made based on ophthalmologic findings. Testing for the three most common mitochondrial DNA mutations may confirm the diagnosis.

Differential Diagnosis

Optic neuritis, compressive optic neuropathy, and infiltrative optic neuropathy.

Prophylaxis

There is no proven prophylaxis; however, it is theorized that avoiding substances such as tobacco and excess alcohol may be beneficial because these substances increase energy demands.

Therapy

Therapy is largely supportive including visual aids, occupational rehabilitation, and genetic counseling. Agents that may increase mitochondrial energy production such as coenzyme Q10 and succinate have been used but without definite success. Antioxidants have also been used without definitive success and corticosteroids are not beneficial. Idebenone has also shown modest improvement in patients with LHON, but currently no proven effective treatment for LHON exists.

Prognosis

The majority of patients have permanent central vision loss in both eyes; however, central vision may eventually improve in 10–20% of patients depending on mutation. The likelihood of spontaneous visual improvement is higher in patients with a mutation at location 14484 than at location 11778.

Epidemiology

LHON affects males more commonly than females. Women account for only 10–20% of cases. The onset of LHON is typically in the age range of 10–30 years; however, it can occur in early childhood or later in adulthood. The prevalence of LHON has been estimated to be 1 in 30,000–50,000 in Northeast England and Finland.

Cross-References

► Optic Neuritis
► Optic Neuropathy

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Leber Hereditary Optic Neuropathy (LHON)

► Mitochondrial Optic Neuropathy

Leber Optic Atrophy

► Leber Hereditary Optic Neuropathy

Leber's Hereditary Optic Neuropathy (LHON)

► Toxic/Nutritional and Hereditary Optic Neuropathy

Ledercort D

► Intravitreal Triamcinolone

Legal Blindness: Definition

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Definition

The degree of poor visual function that qualifies a person as formally blind. This definition is

relevant in case of social security or insurance issues if the patient is severely visually disabled but has a residual visual function. The definition – determined by a visual acuity threshold and other criteria such as visual field defects – is different from country to country.

The U.S. definition states as follows: "An individual shall be considered to be blind for purposes of this title if he has central visual acuity of 20/200 or less in the better eye with the use of a correcting lens. An eye which is accompanied by a limitation in the fields of vision such that the widest diameter of the visual field subtends an angle no greater than 20 degrees shall be considered for purposes of the first sentence of this subsection as having a central visual acuity of 20/200 or less."

The 20/200 threshold (1.0 logMAR) is also used in Australia, while in the UK 20/400 and Germany 20/1000 is used. The level above legal blindness is referred to as severe visual disability.

Lens Capsule

► Capsular Bag

Lens Dislocation

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Synonyms

Phacomorphic angle-closure glaucoma

Definition

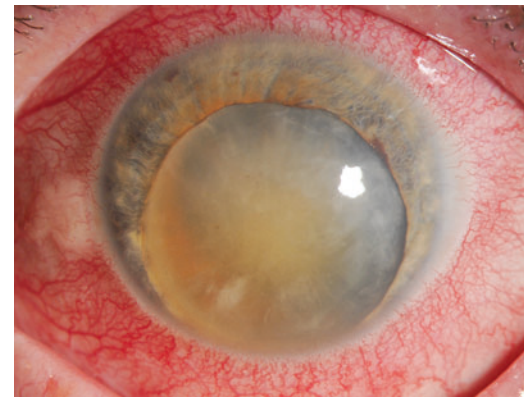
Lens dislocation may cause secondary angle block.

Etiology

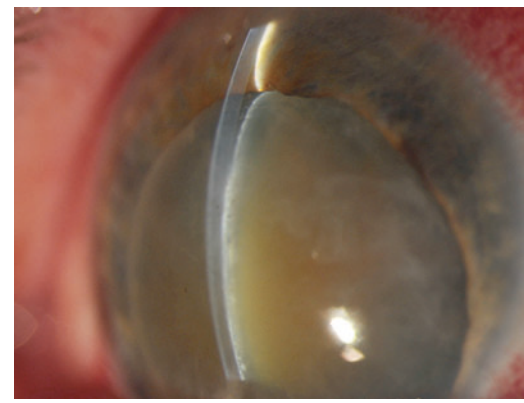
The lens is displaced from its normal anatomic position (ectopia lentis). The reason for the dislocation could be a previous trauma or predisposed insufficient zonula fibers (e.g., PEX, in Marfan syndrome) (Stamper et al. 2009). Anterior displacement of the lens (Figs. 1 and 2) may cause phacomorphic and/or pupillary block configuration (acute mixed mechanism glaucoma).

Causes for ectopia lentis are:

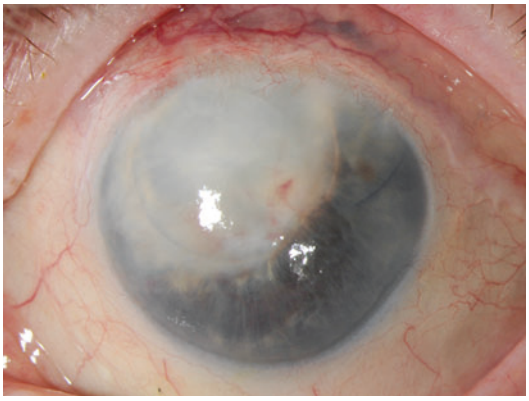
- PEX
- Trauma (Figs. 3 and 4)
- Marfan syndrome
- Homocystinuria (Figs. 5, 6, and 7)
- Microspherophakia
- Weill-Marchesani syndrome (Fig. 8)



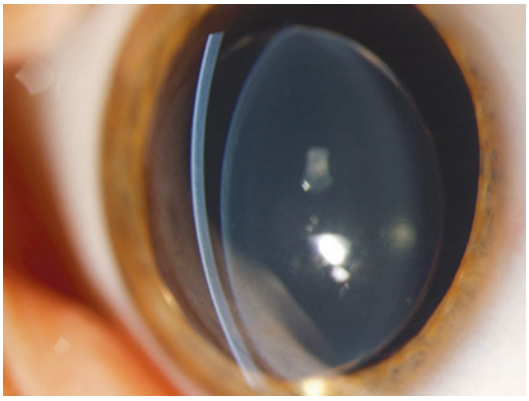
Lens Dislocation, Fig. 1 The lens is anteriorly displaced into the anterior chamber



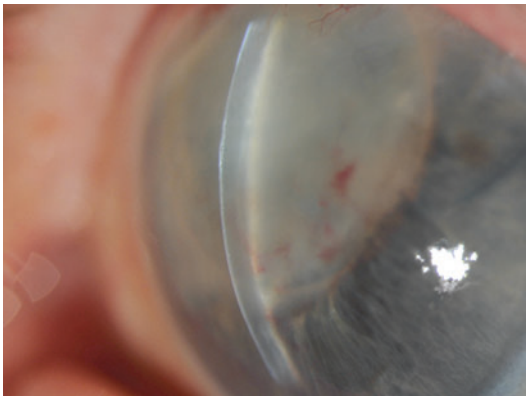
Lens Dislocation, Fig. 2 Slit lamp biomicroscopy shows endothelial-lens-touch with secondary angle obstruction



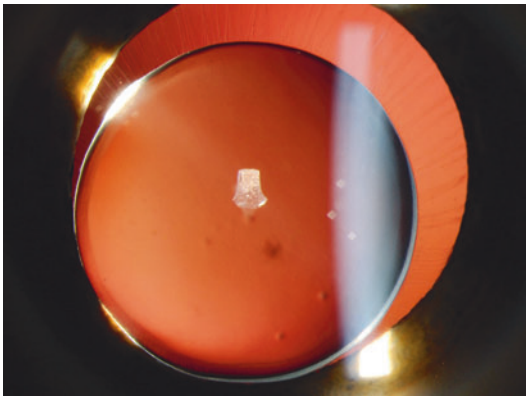
Lens Dislocation, Fig. 3 After trauma, the lens is fully dislocated into the anterior chamber



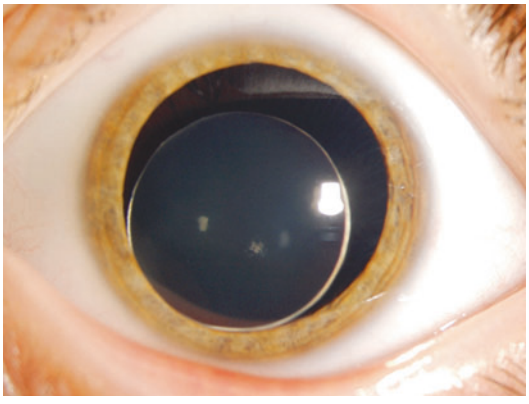
Lens Dislocation, Fig. 6 Anteriorly subdislocation is obvious on slit lamp biomicroscopy examination



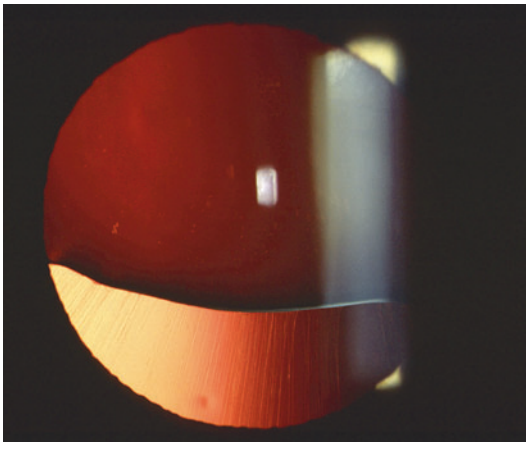
Lens Dislocation, Fig. 4 Endothelial-lens touch after traumatic lens displacement with secondary angle-block



Lens Dislocation, Fig. 7 Overly streched zonulaes visisble in retro-ilumination



Lens Dislocation, Fig. 5 Lens is anteriorly and inferiorly sub-dislocated



Lens Dislocation, Fig. 8 Lens is superiorly sub-dislocated with visable zonulae in retro ilumination

Clinical Presentation

Clinical presentation is similar to any acute angle-closure glaucoma with blurred and reduced visual acuity, halos, and pain.

Diagnosis

A complete luxation of the lens either in the anterior chamber or in the vitreous body is possible. Some lenses are only anteriorly or posteriorly subluxated. In some cases, subluxation of the intraocular lens (IOL) is assumed by deepening of the anterior chamber that is recognized by biomicroscopy, gonioscopy, or ultrasound biomicroscopy (Stamper et al. 2009).

Differential Diagnosis

Pupillary block glaucoma, aqueous misdirection glaucoma, mixed mechanism glaucoma, iris en plateau configuration or syndrome.

Prophylaxis

Early lens extraction in predisposed eyes (e.g., hyperopic eyes, zonule insufficiency, acute phacomorphic block in the fellow eye).

Therapy

Based on the underlying mechanism, peripheral laser iridotomy might not be sufficient. "Clear" lens extraction and implantation of an intraocular lens is the desired treatment to prevent recurrent lens block and damage to the optic nerve (Salehi-Had and Turalaba 2010).

Prognosis

Dependent on the initial damage to the optic nerve.

Epidemiology

- PEX.
- Trauma (often young males).
- Marfan syndrome ca. 1:5000–10,000.
- Homocystinuria ca. 1:200,000.
- Other reasons (e.g., microspherophakia, Weill-Marchesani syndrome) are really rare.

Cross-References

- ▶ Ectopia Lentis
- ▶ Homocystinuria
- ▶ Pseudoexfoliation Syndrome
- ▶ Pseudoexfoliative Glaucoma
- ▶ Traumatic Glaucoma

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Lens Ectopy

- ▶ Ectopia Lentis

Lens Epithelial Cells

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Definition

Lens epithelial cells adhere to the anterior lens capsule and extend to the equatorial lens bow. Their proliferative capacity varies according to their location. At the equator constant cell

division is responsible for the formation of new fibers and lens growth throughout life (Boulton and Saxby 2004).

Histology

Lens epithelial cells have a cuboidal shape and a size of approximately 10 μm height and 15 μm width (Boulton and Saxby 2004). A monolayer of anterior cells (A-cells) with minimal mitotic activity is located on the anterior capsule. These cells can proliferate and undergo a pseudofibrous metaplasia under pathological conditions. The E-cells can be found at the lens capsule equator. These cells are not only very active in terms of mitosis but are also able to proliferate and migrate when traumatized (Apple et al. 1992; Pandey et al. 2004). In the phakic healthy eye, the posterior lens capsule is cell-free.

Electron Microscopy

The nuclei of lens epithelial cells are typically large, and lateral adhesion complexes consisting of tight junctions and desmosomes connect the cells to each other. Cytoskeletal elements are microfilaments (actin), intermediate filaments (vimentin), and microtubules (tubulin) forming a network that controls cell shape as well as different functions within the cells (Boulton and Saxby 2004).

Cross-References

► Capsular Bag Opacification
► Sealed Capsule Irrigation Device

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Lens Extraction

► Lensectomy

Lens Instability

► Luxated Lens

Lens Luxation

► Luxated Lens

Lensectomy

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Synonyms

Lens extraction

Definition

Lensectomy is the surgical extraction of the crystalline lens. This surgical procedure can be

performed as an extracapsular cataract extraction (ECCE) using phacoemulsification or phacofragmentation for the deterioration of the lens by preventing the elastic capsular bag for the implantation of a posterior chamber intraocular lens. Another method for lensectomy is intracapsular cataract extraction (ICCE) done by puncture incision through the ciliary disk. This surgical procedure means the complete removal of the crystalline lens.

Epidemiology

Cataract surgery is the most common surgery worldwide. Detailed data about the incidence of cataract surgery do not exist but there are approximately 18 million operations per year. The frequency and the operation technique varied among developed and undeveloped countries. In the USA nearly 80% of all cataract surgeries are accomplished by phacoemulsification. In undeveloped countries where medical devices are rare, the ICCE (intracapsular cataract extraction) technique is still preferred.

History

Cataract operations are among the oldest recorded surgical procedures; there are references to cataract surgery written around 600 B.C. by Susruta, a famous surgeon from India. In the ancient world, lenses damaged by cataracts were dislocated rather than removed in the strict sense; the surgeon used a lance to push the clouded lens backward into the vitreous body of the eye. Extracapsular cataract extraction by inferior incision and a few years later intracapsular cataract extraction by thumb expression started in the middle of the eighteenth century. In 1967 the elegant method of lensectomy by phacoemulsification was developed and until today this technique is used in most cases of cataract or refractive lensectomy.

Clinical Features

Cataract is clouding of the lens of the eye which impedes the passage of light. Although most cases of cataract are related to the aging process, occasionally children can be born with the condition, or a cataract may develop after eye injuries, inflammation, and some other eye diseases. Gold standard in cataract treatment is the surgical removal of the crystalline lens and the simultaneous implantation of an artificial intraocular lens. In modern cataract surgery, two main surgical techniques dependent on the progression of the cataract can be performed. For further information see treatment section below.

Test

To examine best postoperative results thorough slit lamp examination with dilated pupil, Scheimpflug imaging and measurement of uncorrected and best spectacle-corrected visual acuity are essential.

Etiology

See “Clinical Features” section above.

Treatment

Two main surgical techniques exist for extraction of the crystalline lens. One is called extracapsular cataract extraction (ECCE) and the other is intracapsular cataract extraction (ICCE). Intracapsular cataract expression was performed in former times and this procedure includes the removal of the crystalline lens inclusive the elastic capsule. The eye was left aphakic in this procedure. Since the development of phacoemulsification in the 1970s, intracapsular cataract extraction has not been the procedure of choice because of much higher complication rates such as hemorrhage, vitreous loss, retinal detachment, and cystoid macular edema. Today extracapsular cataract extraction is the most common method for lensectomy. In this method the lens of the eye is removed, while the elastic capsule that covers the lens is left partially intact to allow implantation of an intraocular lens (IOL). Two main types of ECCE exist: manual expression, in which the

lens is removed through an incision made in the cornea or the sclera of the eye, and phacoemulsification, in which the lens is broken into fragments inside the capsule by ultrasound energy and removed by aspiration.

Cross-References

- ▶ Cataract Eye Operation
- ▶ Phacoemulsification and Posterior Chamber Intraocular Lens (IOL) Implantation

Further Reading

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Lens-Induced Angle-Closure Glaucoma

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Synonyms

Acute angle closure in dislocated or intumescent lens

Definition

Two different disorders of the crystalline lens are associated with angle-closure glaucoma (Allingham et al. 2005). Firstly, angle-closure glaucoma may be associated with dislocation of lens. In these conditions the lens may be either subluxated or completely dislocated into the anterior chamber. The dislocation of the lens may be traumatic (which is the most common cause), after minor trauma (as in pseudoexfoliation syndrome), spontaneous, or due to inherited abnormal position of the lens with or without other ocular or systemic abnormalities. Secondly, in eyes with advanced cataract formation, the lens may become swollen or intumescent, with progressive narrowing of the anterior chamber angle eventually leading to a form of angle-closure glaucoma, referred to as phacomorphic glaucoma (Tarongoy et al. 2009).

Etiology

The mechanism of angle-closure glaucoma in cases with subluxated or dislocated lenses is usually pupillary block. The lens may block aqueous flow through the pupil if it is dislocated into the pupil or anterior chamber or if it is subluxed or tilted forward against the iris without entering the anterior chamber. Pupillary block may also be associated with a dislocated lens due to herniation of vitreous into the pupil. Peripheral anterior synechia may develop from long-standing pupillary block and produce chronic IOP elevation. In eyes with advanced mature or hypermature cataracts, as rarely seen in developed countries but quite common in the second or third world, the angle closure may be caused by an enhanced pupillary block mechanism or by forward displacement of the lens-iris diaphragm.

Clinical Presentation

Mainly blunt trauma to the eye can cause dislocation of the lens. The patients present with pain and blurred vision mainly due to the IOP increase. The subluxation of the lens may be initially missed but a very deep anterior chamber should raise the suspicion. In cases of traumatic dislocation of the lens, concomitant trauma to the anterior chamber angle from the initial injury may be the cause of the associated glaucoma. A transient pressure elevation may persist for days or weeks after traumatic dislocation of the lens. In some older individuals, dislocation of the lens may occur spontaneously, usually in association with cataract formation. Spontaneous dislocation has

also been reported in eyes with high myopia, uveitis, buphthalmos, or megalocornea.

Simple ectopia lentis is usually inherited by autosomal dominant mode. The condition is usually bilateral and symmetric, with lens dislocation generally upward and outward and occasionally into the anterior chamber. Ectopia lentis and pupillae is a rare, autosomal recessive condition characterized by small, subluxated lenses and by oval- or slit-shaped pupils that are displaced usually in the opposite direction from that of the lens. The condition is usually bilateral, although marked variation may be seen between eyes of the same patient. The condition is associated with a wide variety of other ocular abnormalities including severe axial myopia, iris transillumination defects, poor pupillary dilatation, and glaucoma. The pathogenesis of this disorder is unknown. Ectopia lentis can also be seen with systemic abnormalities in Marfan syndrome, homocystinuria, and Weill-Marchesani syndrome and other rare congenital disorders including Ehlers-Danlos syndrome, hyperlysinemia, sulfite oxidase deficiency, and aniridia.

Patients with mature or hypermature cataract will present with symptoms very similar to acute angle-closure glaucoma, i.e., redness, pain, grossly reduced visual acuity, and quite often corneal edema. Intraocular pressure is significantly elevated, often exceeding 30–40 mmHg. As this condition is more often seen in the second or third world, there is usually a marked delay in diagnosis, and patients may present with a history of vision loss for several weeks or months.

Diagnostics

In cases with ectopia lentis, slit-lamp examination may reveal lenticular subluxation and dislocation. If zonules are weak, then phacodonesis or iridodonesis may also be present. The nature of the zonular defect may be revealed by ultrasound biomicroscopy (UBM), which enables in vivo imaging of the zonules and can detect zonular loss and stretching directly. In the region of zonular disorders, the lens shows increased lenticular sphericity, which may also be seen clinically.

In cases of phacomorphic angle-closure glaucoma, the diagnosis is usually made by observing a mature, intumescent cataract associated with a central anterior chamber depth that is significantly shallower than that of the fellow eye. The fellow eye, however, may also show a shallow anterior chamber and a gonioscopic angle width of less than 20°.

Differential Diagnosis

In some cases, the lens may dislocate completely into the vitreous cavity and later undergo degenerative changes with release of material that obstructs aqueous outflow. Phacolytic (lens protein) glaucoma may also be seen in patients with advanced cataracts without luxation of the lens. In these cases the chamber angle is open, and there is a marked anterior inflammation with heavy flare in association with iridescent or hyperrefringent particles (calcium oxalate or cholesterol) and sometimes extremely large round cells (macrophages). Lens particle glaucoma after disruption of the lens capsule by cataract extraction or penetrating injury is easily distinguishable by the "fluffed-up" lens cortical material in the anterior chamber. Phacoanaphylaxis with retained nucleus fragments in the vitreous after complicated cataract surgery is easily distinguished because of a chronic, relentless, granulomatous-type inflammation that centers on lens material.

Prophylaxis

In cases with subluxated or luxated lenses, the removal of the lens should be considered as prophylaxis of angle-closure glaucoma. Prophylactic iridotomy in cases of microspherophakia has also been advocated to avoid pupillary block glaucoma. Phacomorphic glaucoma is rarely seen in developed countries because usually cataract surgery is performed before the cataract is mature. Some grade of phacomorphic angle narrowing due to increased thickness and more anterior position of the lens may also be present in a majority of cases

with acute (pupillary block) or chronic angle-closure glaucoma; thus, cataract surgery in these cases has become popular. In eyes with primary angle closure, cataract surgery opened the angle concomitant with the attenuation of the anterior position of the ciliary processes (Nonaka et al. 2006).

Therapy

If the lens is displaced anteriorly in the anterior chamber or partially through the pupil, it may be possible to relieve the condition by dilating the pupil and allowing the lens to reposit back into the posterior chamber. Miotics should be avoided when the pupillary block is caused by loose zonules. If the lens is totally dislocated in the anterior chamber, surgical removal of the lens is indicated. Cycloplegics may help to break the attack by pulling the lens posterior. Hyperosmotic agents, carbonic anhydrase inhibitors, or topical beta-blockers may also be useful in breaking the attack. The definite treatment however is a laser iridotomy. The iridotomy should be placed peripherally to avoid subsequent obstruction by the lens. Argon laser peripheral iridoplasty (ALPI) may also be helpful in some cases of angle-closure glaucoma without a significant pupillary block component (Ritch et al. 2007). The extraction of a subluxated lens is associated with increased surgical risk but should be performed if the lens is in the anterior chamber or lens extraction is needed to relieve the glaucoma or improve vision.

In phacomorphic glaucoma, the treatment is initial medical reduction of the IOP with hyperosmotics, carbonic anhydrase inhibitors, and topical beta-blockers or alpha2-agonists, followed by extraction of the cataract. ALPI is also effective as an initial treatment to break attacks of acute phacomorphic angle closure. In acute phacomorphic angle closure, the eye is very often severely inflamed, as these patients have usually been referred after being treated unsuccessfully for a few days. Breaking the attack with ALPI may allow a week more for the inflammation and folds in Descemet's to clear, permitting cataract extraction under conditions much closer to ideal. Any element of pupillary block is treated with iridotomy as soon as possible (usually within 2–3 days) after breaking the attack.

Prognosis

In cases with subluxated or luxated lenses, the prognosis is dependant on the nature of the causing condition (i.e., severity of the trauma) and the duration and amount of IOP elevation. Immediate diagnosis and adequate treatment is mandatory. In patients with phacomorphic glaucoma, especially often seen in less developed countries, the distance from the hospital, duration of pain, and high level of IOP at presentation were all associated with poor visual outcome (Pradhan et al. 2001). Under these conditions even with very experienced cataract surgeons, only one third of patients regained useful (6/60 or better) visual acuity.

Epidemiology

The major cause of lens-induced angle-closure glaucoma in developed countries is blunt ocular trauma. Inherited ectopia lentis is rare; the most common form is Marfan syndrome. Phacomorphic angle closure is also very rare in the first world, but is not so rare in the second and third world. In a prospective series of 27073 cataract surgeries performed during a 1-year period in a single hospital in southeast Nepal, 296 eyes (1%) presented with phacomorphic glaucoma.

Cross-References

- Homocystinuria
- Marfan Syndrome
- Ocular Pressure Patch
- Weill-Marchesani Syndrome

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Lensmeter

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Synonyms

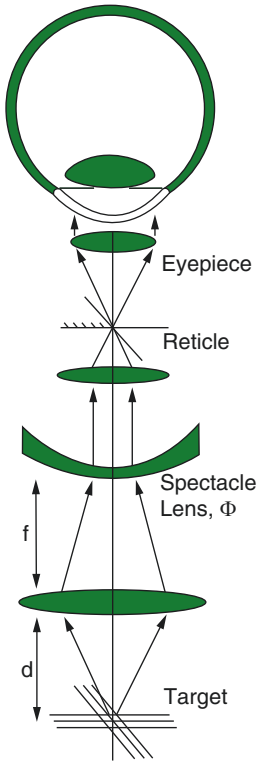
Focimeter; Lensometer

Definition

A lensmeter is a device for measuring the power of a spectacle lens. A target (typically a crossed set of lines) is imaged through a lens of focal length f. The spectacle lens under test is placed at the rear focal point of this lens. Light emerging from the spectacle lens enters an eyepiece with an internal reticle. The user axially shifts the target until it is simultaneously in focus with the reticle. This situation occurs when the light emerging from the spectacle lens is collimated. The target position d is related to the power of the spectacle lens Φ by:

Lensmeter Equation

The target can be rotated to align with the axes of a spherocylinder lens. When cylinder is present, only one set of target lines can be in focus. Readjusting the lensmeter will bring the orthogonal set of lines into focus. The difference in power between the two focus positions is the cylinder power of the lens. The different zones of a progressive addition lens can also be measured with a lensmeter by shifting the position of the lens in front of the aperture of the eyepiece. Modern versions of the device are automated.



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Lensometer

▶ Lensmeter

Lenticonus

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Definition

Lenticonus is a local bulging of the capsule of the crystalline lens and the underlying lens cortex. It commonly occurs at the anterior or posterior pole of the lens.

Posterior lenticonus is a congenital defect which is limited to the eye and not associated with systemic diseases. Recently, an association of posterior lenticonus with microcornea, persistent fetal vasculature, and coloboma has been described.

Anterior lenticonus is bilateral, acquired, and in most cases associated with Alport's syndrome of nephrotic hematuria and deafness. It is believed to be a manifestation of a generalized basement membrane disorder. Associations of anterior lenticonus with Lowe's and Waardenburg's syndrome have also been described.

Histology

Histological examinations of the capsule in lenticonus showed a thinned and ectatic anterior capsule with accumulation of collagen type IV and type VI and irregular arrangement of collagen fibers. Lens cortical material was found to be protruded into the capsular ectasia (van Setten 2001).

Immunohistochemistry

Immunohistochemistry provided evidence for a defect of the a3 to a6 chains of type IV collagen in anterior lenticonus associated with Alport syndrome (Ohkubo et al. 2003).

Electron Microscopy

Electron microscopy of the lens capsule in anterior lenticonus after cataract surgery revealed abnormal thinning of the capsule and capsular breaks (Junk et al. 2000).

Molecular Diagnostics

Patients with lenticonus associated with Alport syndrome show mutation of genes encoding collagen synthesis, most commonly the COL4A5 gene (Ohkubo et al. 2003).

Differential Diagnosis

The condition is detectable by slitlamp examination. Patients should be examined for associated abnormalities, especially Alport syndrome. Similar appearance of the lens may be caused by ocular trauma.

Cross-References

▶ Cataract, Causes and Treatment
▶ Lens Capsule

References

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Lentigo Senile (Liver Spots)

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Synonyms

Lentigo simplex; Liver spots; Solar lentigo; Sun spots

Definition

Flat, evenly pigmented benign cutaneous lesions.

Etiology

Chronic sun exposure, resulting in an increased number of melanosomes.

Clinical Presentation

A macule with uniform pigmentation. They are usually 5 mm in size, flat, and increase in size and number with age. Lesions become darker with increased sun exposure. They occur frequently on the forehead and back of the hands.

Diagnostics

Excisional biopsy is not necessary; however, suspicious lesions may be excised to distinguish them from other melanocytic lesions.

Differential Diagnosis

Ephelides
Lentigo simplex
Nevus
Melanoma

Prophylaxis

Appropriate UV-protection and sunscreens may decrease the appearance and pigmentation of senile lentigo.

Therapy

Treatment in not necessary; however, suspicious lesions may be biopsied to distinguish it from other melanocytic lesions. Topical melanin bleaching creams, cryotherapy, and chemical peels may improve cosmetic appearance.

Prognosis

Prognosis for senile lentigo is excellent.

Epidemiology

More common in fair-skinned individuals. They have been reported in 90% of Caucasians by age 60 in the USA (Montagna et al. 1980; Albert and Jakobiec 2008).

Cross-References

▶ Ephelis
▶ Lentigo Simplex

References

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Lentigo Simplex

▶ Lentigo Senile (Liver Spots)
▶ Lentigo Simplex (Simple Lentigines)

Lentigo Simplex (Simple Lentigines)

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Synonyms

Juvenile lentigo; Lentigo simplex; Simple lentigo

Definition

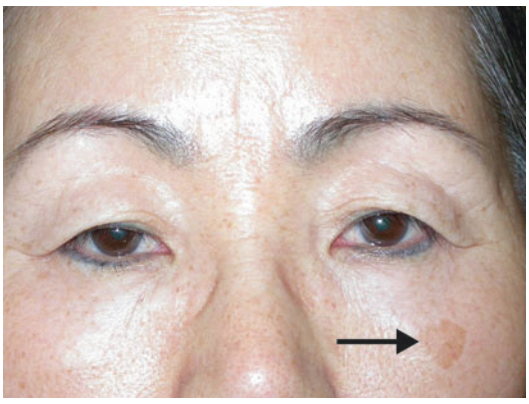
A flat, pigmented benign lesion, typically found on sun-protected skin.

Etiology

A result of an increased number of melanosomes and increased melanin in basal keratinocytes. It does not appear to be related to sun exposure.

Clinical Presentation

Lentigo simplex presents as evenly pigmented round spots, with jagged or smooth borders (Fig. 1). Lesions tend to be 3–15 mm in size and first appear in childhood.



Lentigo Simplex (Simple Lentigines), Fig. 1 Left cheek well circumscribed lesion (*arrow*) representing lentigo simplex

Eyelid lentigines may be associated with Peutz-Jeghers syndrome, an autosomal dominant disorder characterized by benign harmartomatous polyps of the gastrointestinal tract, also known as hereditary intestinal polyposis syndrome (Albert and Jakobiec 2008).

Diagnostics

Excisional biopsy is not necessary.

Differential Diagnosis

Ephelides
Actinic Keratosis
Seborrheic Keratosis

Prophylaxis

No prophylaxis is known.

Therapy

Treatment is not necessary. Topical melanin bleaching creams may improve cosmetic appearance.

Prognosis

Excellent

Epidemiology

Lentigo simplex is the most common form of lentigo.

Cross-References

▶ Ephelis
▶ Solar Lentigo

References

Albert D, Jakobiec F (2008) Principles and practice of ophthalmology, 3rd edn. Saunders, Philadelphia, p 3747

Leprosy

▶ Hansen's Disease

LESCs: Limbal Epithelial Stem Cells

▶ Limbal Stem Cells

Lesions of the Optic Chiasm

▶ Chiasmal Disorders

Letter-Box Technique

▶ Can-Opener Technique

Levator

▶ Levator Muscle (Levator Palpebrae Superioris)

Levator Muscle (Levator Palpebrae Superioris)

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Synonyms

Levator

Definition

The levator is a skeletal muscle responsible for voluntary elevation of the upper eyelid.

Structure

The levator originates at the lesser sphenoid wing of the orbital apex and travels along the underside of the orbital roof (just above the superior rectus muscle) as it extends forward. At the aperture of the orbit, it is supported by the superior transverse orbital ligament of Whitnall and changes from a muscular structure into a fibrous aponeurosis. The aponeurosis extends inferiorly in the eyelid and inserts on the tarsal plate. As the aponeurosis extends inferiorly, it broadens to form the medial and lateral horns which distribute the forces of the levator muscle. The aponeurosis sends out multiple delicate fibers forward and downward through the orbicularis muscle to insert onto the interfascicular septa of the orbicularis muscle and subcutaneous tissue to create the upper eyelid crease. The levator muscle is innervated by the superior division of the third cranial nerve.

Function

It is the primary retractor of the upper eyelid.

Clinical Relevance

Assessment of the function of the levator muscle is crucial when evaluating ptosis. Levator function is measured as the millimeters of movement during eyelid excursion from extreme downgaze to extreme upgaze. Normal levator function is about 15 mm and is an indicator of normal strength of the muscle. In congenital ptosis, levator function is reduced, but in involutional ptosis, normal levator function is maintained. In addition, the appearance of the eyelid crease can aid in differentiating these two main types of eyelid ptosis. In congenital ptosis, the eyelid crease is not well defined, but in involutional ptosis, it is high.

The etiologies of these two disorders explain the above findings. In congenital ptosis, the levator muscle is abnormal, weak, and fibrotic; therefore, it does not move well upward or downward. In primary gaze, the lid is low, and in downgaze, the lid often shows lid lag. In involutional ptosis, the muscle itself is normal, but the aponeurosis

either is disinserted from the tarsal plate or is stretched. This abnormality results in normal measurements of levator function but a high eyelid crease as the tiny fibers of the aponeurosis drag the skin upward. In downgaze, the lid margin remains low as the eyelid is effectively lengthened by the stretched or disinserted aponeurosis.

The levator muscle may also be relevant to the eyelid retraction which can be associated with Graves' disease, as one proposed mechanism for this finding is infiltration and fibrosis of the levator muscle.

Cross-References

- ▶ Proptosis
- ▶ Whitnall's Ligament

Further Reading

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Lhermitte Peduncular Hallucinosis

▶ Peduncular Hallucinosis

LHON

▶ Leber Hereditary Optic Neuropathy

Lid Biopsy

▶ Full-Thickness Eyelid Biopsy

Lid Sharing Procedure

▶ Cutler-Beard Procedure

▶ Hughes Procedure/Modified Hughes Procedure, in Eyelid Repair

Light Adaptation

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Definition

The process by which the retina reduces its sensitivity to light as ambient light is increased.

Structure

Light adaption occurs predominantly in retinal cone cells. It appears to be absent or only minimally present for retinal rod cells in isolation. Nonetheless, retinal rod cells in vivo do appear to demonstrate a wide range of voltage excursions independent of ambient light conditions and thus apparently benefit from the light adaption ability of retinal cone cells (Miller 2006).

Function

Light adaption allows eyes to maintain ideal vision throughout a wide range of illumination conditions. Under typical conditions, an object is visible due to the difference in reflected light from itself as compared to its surroundings, also known as contrast. As the ambient light increase, the absolute difference in reflected light changes, but the ratio of reflected light remains the same. Light adaption provides eyes with a mechanism to maintain vision based on ratio of reflected light rather than absolute amount of reflected light. In animal experiments, light adaption allowed eyes to maintain a stable contrast ratio even though ambient illumination changed by a factor of 50,000.

Clinical Relevance

Light adaption is essential for maintaining ideal vision across a wide range of ambient

light conditions as described above. Since the main mechanisms for this ability involves bleaching of pigments in photoreceptor cone cells, light adaption may be malfunctional in any cell with abnormal photopigments or bleaching mechanisms. Additional mechanisms for light adaption probably also exist. However, these appear to be most influential at low light conditions and likely involve alterations in cGMP and calcium ion channel levels (Miller 2006).

Light adaption directly influences all results from any electrophysiological testing of the retina, including electroretinogram, electrooculogram, and dark adaptation testing (Lam 2005). It is therefore paramount that the process of light adaption be standardized for all labs so that reliable and consistent results are obtained.

It should be noted that light adaption is simply not the converse of dark adaption. Dark adaption occurs over a slower time frame than light adaption and involves regeneration of photopigment in retinal rods and cones, rather than bleaching of photopigments.

Cross-References

► Dark Adaptation Testing
► Peripheral Retina

References

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Light Toxicity

► Light Toxicity, Free Radical Damage; Photic Damage/Phototoxicity, Free Radical Damage

Light Toxicity, Free Radical Damage; Photic Damage/Phototoxicity, Free Radical Damage

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Synonyms

Free radical damage; Light toxicity; Photic damage; Phototoxicity

Definition

Thermal, chemical, or mechanical damage to the retina as a result of exposure to visible or ultraviolet light.

Structure

Being a structure designed to receive images of incoming light energy, the eye contains inherent defense mechanisms to protect itself against damage from high light levels. In certain situations, however, these mechanisms can be overwhelmed, and the retina suffers permanent damage if light energy is high enough.

Function

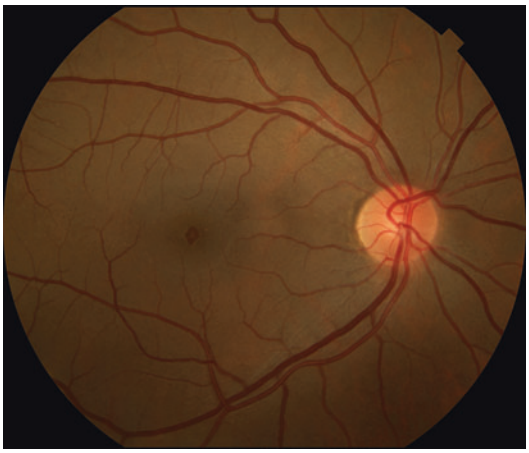
The manifestation of light toxicity depends on the energy level of incoming light and which ocular structures absorb the energy (Gass 1997). Photothermal (photocoagulation) injury involves the absorption of light by melanin in the retinal pigment epithelium and choroid with the subsequent conversion of this energy to heat. If heat production elevates tissue temperature more than 10° Centigrade, proteins denature and produce cell damage, tissue inflammation, and cell death. Photochemical injury develops when incoming light

produces large amounts of free oxygen radicals or singlets which react with ocular tissue. Photomechanical (photodisruption) damage occurs when extremely powerful light energy produces rapid expansion of water vapor or the ionization of ocular tissue, which mechanically disrupts tissue structure.

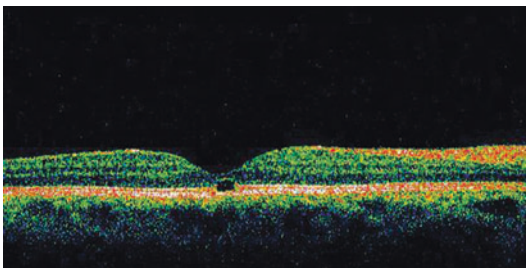
Clinical Relevance

Light injury to the retina is a well-known cause of permanent vision loss. Most cases develop following exposure to solar light, laser light, operating microscope light, or welding arc light. Solar retinopathy classically develops following prolonged sun gazing with dilated pupils (Mainster and Turner 2006). Clinical findings include bilateral small yellowish foveolar lesion that fade over several weeks, eventually producing foveolar retinal pigment epithelium atrophy. Optical coherence tomography demonstrates a characteristic hyporeflective space in the outer retina. Visual acuity is usually diminished to the 20/40 through 20/100 range shortly following light exposure but may improve to the 20/20 through 20/40 range over 6 months. Clinical signs of laser light retinopathy vary according to size and intensity of laser beam but generally include foveolar pigment mottling. Operating microscope light toxicity appears as an oval area of retinal pigment mottling several days following intraocular surgery. Welding arc light toxicity appears similar to solar retinopathy (Figs. 1 and 2).

The photic damage of cumulative light exposure in the aging processes of cataract and age-related macular degeneration progression remains unclear. Some studies do suggest that increased sunlight and ultraviolet ray exposure accelerates disease progression, but this effect has been difficult to objectively measure. Currently, intraocular lenses are manufactured with a blue-absorbing and ultraviolet-absorbing coating to help reduce retinal light damage. Sunglasses and a wide brimmed hat may also be helpful for reducing cumulative ultraviolet exposure to one's eyes.



Light Toxicity, Free Radical Damage; Photic Damage/Phototoxicity, Free Radical Damage, Fig. 1 Color fundus photograph demonstrating foveal abnormality of solar toxicity (Photo courtesy of Thomas B. Connor, Jr.)



Light Toxicity, Free Radical Damage; Photic Damage/Phototoxicity, Free Radical Damage, Fig. 2 Optical coherence tomography of an eye with solar retinopathy demonstrating characteristic hyporeflective space in the outer retina (Photo courtesy of Thomas B. Connor, Jr.)

Cross-References

- ▶ Arc Welding, Occupational Light Injury and
- ▶ Photocoagulation
- ▶ Photodisruption
- ▶ Retinal Tears
- ▶ Retinal Pigment Epithelium

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Light, Pupillary Response

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Synonyms

Pupillary light reflex

Definition

The simultaneous and equal constriction of both pupils to light is mediated by an ipsilateral direct response and a contralateral consensual response.

Structure

The structures comprising the afferent limb of the pupillary light reflex in sequential order include the retina, optic nerve, optic chiasm, optic tract, and pretectal nuclei. The Edinger-Westphal nuclei (EWN), preganglionic parasympathetic fibers, ciliary ganglion, postganglionic parasympathetic fibers, sphincter muscle of the iris comprise the efferent pupillary pathway.

Function

The pupillary light reflex has an afferent and an efferent pathway. The afferent pathway begins when light is shone on the eye and activates neurons in the retina. These neurons then send impulses through the optic nerve (CN II) to the optic chiasm where they are carried bilaterally to the optic tracts. Just prior to the lateral geniculate nuclei, fibers branch off of the optic tract and synapse in the pretectal nuclei at the level of the superior colliculus. From the pretectal nuclei, fibers arise and pass to the ipsilateral and contralateral EWN. Here, efferent preganglionic parasympathetic fibers arise and exit the brainstem with the oculomotor nerve (CN III). These fibers synapse in the ciliary ganglion and give rise to the postganglionic short ciliary nerves which go on to innervate the iris sphincter.

Clinical Relevance

The pupillary light reflex can be quickly and easily assessed clinically by shining a handheld light obliquely, from below the nose, into one eye and carefully observing the pupillary response in both eyes. After several seconds the light can be shined in the other eye again while observing the pupillary response in both eyes (i.e., swinging flashlight test). Ideally, this testing should be performed in a dim room and the pupil size can be measured using a pupillary measuring gauge.

The patient should be instructed to look at a distant object to avoid accommodative pupillary constriction. In a normal exam, shining a light into one eye will cause simultaneous and equal constriction of both pupils. The pupillary light reflex is abnormal if one or both of the pupils does not constrict as much as expected and dilates in response to direct stimulus after swinging the light from the normal pupil to the abnormal pupil with the relative afferent pupillary defect (RAPD). Damage to the parasympathetic efferent pathway produces poorly reactive or unreactive pupil(s) and anisocoria that is worse in the light.

Cross-References

- ▶ Accommodation, Functional (Nonorganic/Nonphysiologic) Disorders of
- ▶ Afferent Pupillary Defects, Relative (Marcus Gunn Pupil)
- ▶ Anisocoria: Big Pupil
- ▶ Anisocoria of the Small Pupil
- ▶ Argyll Robertson Pupil
- ▶ Light-Near Dissociation
- ▶ Pupillary Light Reflex
- ▶ Swinging-Light Test, for RAPD Identification

Further Reading

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Light-Induced Retinal Damage

▶ Electromagnetic Energy/Radiation, Adverse Effects on Retina

Light-Near Dissociation

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Definition

Light-near dissociation occurs when near stimulus produces pupillary constriction that exceeds pupillary constriction in response to bright light.

Etiologies

Light-near dissociation is a pathologic finding with several possible etiologies including severe loss of afferent light input to both eyes, a lesion of the dorsal midbrain, tonic pupils, aberrant reinnervation of the third nerve or ciliary ganglion fibers, and Argyll Robertson pupils.

Severe loss of afferent light input to both eyes, such as a bilateral optic neuropathy, is a common cause of light-near dissociation. There is absent or diminished light reflex due to the reduced light impulses being carried to the pretectal nucleus; however, these patients often retain the ability to

determine object distance and have an intact near reflex. A lesion of the dorsal midbrain can result in light-near dissociation by compressing and interrupting the more dorsally located fibers of the light reflex pathway and sparing the more ventrally located fibers of the near reflex pathway. A dorsal midbrain lesion can also be associated with bilateral eyelid retraction (Collier sign), vertical gaze palsy, accommodative paresis, and convergence-retraction nystagmus. These findings together are known as the Parinaud syndrome.

Light-near dissociation can also result from aberrant regeneration of damaged nerves, which can restore the near reflex but not the light reflex. In normal physiology, the ciliary ganglion sends 30 times more nerve fibers to the ciliary muscle than the iris sphincter. Following damage to the ciliary ganglion, regrowth of ciliary nerves can produce reinnervation of the iris sphincter instead of the ciliary muscle. Thus, nerves that previously innervating the ciliary body as part of the near reflex subsequently innervate the iris sphincter and preserve pupillary constriction in response to near stimuli. This process leads to what is known as Adie tonic pupil when idiopathic; however, injury to the oculomotor nerve from trauma, compression, or infections can produce similar clinical manifestations of light-near dissociation.

Argyll Robertson pupil is a manifestation of neurosyphilis. Affected patients have small (<2 mm), often irregular, pupils that exhibit light-near dissociation (small to pinpoint). While the pupils do not react well to light, the near response and subsequent re-dilation are described as normal and brisk. The briskness of the pupillary movement helps distinguish the Argyll Robertson pupil from a chronic-tonic pupil, which has a slow and sustained tonic response. Adie tonic pupils, as described earlier, can become chronic and more miotic-tonic pupils over time (i.e., little old Adie pupils). Although classically described as related to syphilis, Argyll Robertson-like pupils can occur in patients with diabetes, chronic alcoholism, encephalitis, and following panretinal photocoagulation.

Cross-References

- ▶ Adie's Pupil (Tonic Pupil), Pharmacologic Testing
- ▶ Argyll Robertson Pupil
- ▶ Parinaud (Dorsal Midbrain) Syndrome

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Ligneous Conjunctivitis

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Definition

Ligneous conjunctivitis is a recurring, chronic conjunctivitis in which an absence of plasmin results in an inability to break down fibrin clots resulting in the accumulation of fibrinous pseudomembranes on the conjunctiva. This disease process may be associated with systemic pseudomembranes involving the gingiva, ears, respiratory tract, female genital tract, and renal collecting system.

Etiology

Ligneous conjunctivitis is the most common manifestation of type 1 plasminogen deficiency, also known as hypoplasminogenemia. The consequence of decreased plasminogen is a decreased

in plasmin which results in an inability to break down fibrin clots. Thus, wound healing is usually halted at the stage of granulation tissue formation. Ligneous conjunctivitis is usually an autosomal recessive disease stemming from a mutation on chromosome 6q26. Episodes may be triggered by relatively minor trauma or systemic factors such as antifibrinolytic therapy or fever.

Clinical Presentation

Patients may initially present with a nonspecific conjunctivitis in childhood, with a median age of 5 years old. However onset may occur at any age. Ligneous conjunctivitis can present in children of all ethnic groups. Usually, lesions involve the upper palpebral conjunctiva, but may also involve the bulbar and lower palpebral conjunctiva. Lesions generally have a red or yellowish-white appearance and a woody texture, hence the name ligneous, which means consisting of or resembling wood. The lesions can be covered in a thick yellow-white mucoid discharge. This disease may be precipitated by infection, surgery, or trauma. Fifty percent of cases are bilateral. In 30% of cases, the disease progresses to an advanced stage where the cornea is affected. This involves corneal scarring, vascularization, infection, or melting. Although systemic lesions are less common, other sites where lesions can present are the ears, respiratory tract, female genital tract, skin, and renal collecting system. There have been several reports of children with the disease developing hydrocephalus. Ligneous conjunctivitis has also been linked to congenital hydrocephalus and juvenile colloid milium.

Diagnosis

Ligneous conjunctivitis may be initially diagnosed clinical initially based on the patient's history and examination of the eye. However, but it may be confirmed with laboratory data demonstrating decreased plasminogen activity. Pathology specimens demonstrating pseudomembranes with a fibrin-rich component further indicate this diagnosis. A positive family history of ligneous conjunctivitis or involvement in other mucosal sited also can serve to help make this diagnosis.

Differential Diagnosis

The differential diagnosis for ligneous conjunctivitis includes any infectious or inflammatory entity which can cause a chronic pseudomembranous conjunctivitis. These could include amyloidosis, allergic or vernal conjunctivitis, bacterial conjunctivitis (including chlamydia, diphtheria, staphylococcus, and streptococcus), toxic conjunctivitis (secondary to medication use), and viral conjunctivitis (including herpes simplex virus, molluscum contagiosum, or adenovirus-type epidemic keratoconjunctivitis). It is especially important to submit any surgically excised pseudomembranes to pathology to confirm the subepithelial, eosinophilic deposits of fibrin-rich material. This will rule out amyloid, as amyloidosis can mimic this disease closely.

Prophylaxis

There is no prophylaxis for this disease entity as it is genetic in nature.

Therapy

Although the current treatment of choice is plasminogen replacement, historically, treatment success rates of 75% were achieved with surgically removing lesions with careful diathermy at the base of lesions and long-term post-op care. Once the pseudomembranes have been removed, hourly heparin and steroid treatments are begun immediately. This is continued until the wound has reepithelialized. Over the next few weeks, these treatments are then tapered until all signs of inflammation have disappeared. It has been noted that recurrence may be delayed with long-term cyclosporine and steroid administration.

Other treatment modalities such as amniotic membrane transplantation onto the conjunctiva following removal of the lesion have also been tried but with less success. Early recurrence of the ligneous lesions will result if appropriate postoperative care is not given to stem any inflammation or fibrin clotting.

Of note topical plasmin has been shown to be ineffective, because it is rapidly broken down in the tear film. Unfortunately commercial plasminogen concentrate is not currently available for local or systemic treatment. When creating a treatment plan for patients with ligneous conjunctivitis, a hematologist should also be included in management.

Prognosis

Untreated, ligneous conjunctivitis can persist for decades. Spontaneous resolution of lesions is rare. With the older treatment of surgical removal of conjunctival lesions with diathermy followed by weeks of steroid and heparin treatments, success rates of up to 75% have been reported. Currently, with systemic IV therapy of plasminogen, patients are achieving even higher rates of success.

Patients should have close follow-up to monitor for any recurrence of pseudomembranes. Patients will still be at risk for recurrence even years later. Polycarbonate glasses may be helpful in protecting the eyes from environmental trauma and initiating the cascade of damage and repair mechanisms that can release fibrin and cause another episode of ligneous conjunctivitis to recur.

Ultimately, the prognosis of this disease depends on the ability to control the inflammation and recurrence of pseudomembranes. Poorer outcomes are indicated in patients with corneal involvement. In young children, this corneal scarring could result in amblyopia. Topical steroid in the postoperative setting to decrease inflammation can also lead to steroid-induced ocular hypertension. Systemic disease, with respiratory tract pseudomembrane formation, can be life threatening.

Epidemiology

Ligneous conjunctivitis usually presents in infants or young children of all ethnic groups. There is a slight female preponderance. The median age of presentation is 5 years old, but it can present at any age.

Cross-References

▶ Conjunctivitis
▶ Keratoconjunctivitis: Overview

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Limbal Autograft/Allograft (Limbal Transplantation)

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Synonyms

Keratolimbal autograft/allograft

Definition

Conjunctival limbal autografting (CLAU) is a procedure that involves the transplantation of

autologous conjunctival and limbal tissue from the contralateral unaffected eye into the limbal stem cell-deficient eye. In contrast, the transplantation of keratolimbal tissue from either cadaveric eyes or living related donors is done in keratolimbal allograft surgery (Liang et al. 2009).

Indication

The limbal stem cell compartment, located at the palisades of Vogt, is responsible for renewal of the corneal epithelium. The corneal epithelium possesses both a critical barrier function, as well as promoting stability in the tear film (Krachmer et al. 2010; Weisenthal et al. 2013). Limbal stem cell deficiency (LSCD) arises due to either congenital or acquired causes. Congenital causes include aniridia, sclerocornea, and xeroderma pigmentosa. Acquired etiologies typically involve either destruction of limbal stem cells or dysfunction of the limbal stem cell compartment. Common acquired causes include contact lens wear, chemical/thermal burns, autoimmune (Stevens-Johnson syndrome, ocular cicatricial pemphigoid), severe dry eye disease, infections, and neoplasms (Ahmed 2012).

The barrier function of the limbus is lost in LSCD. As a result, conjunctival cells migrate onto the cornea, leading to conjunctivalization of the corneal surface. This conjunctivalization is often associated with neovascularization (both deep and superficial). Persistent epithelial defects and surface irregularity also arise due to compromised epithelial wound healing.

Mild cases of LSCD may be treated by removal of underlying triggers and with topical steroids, scleral contact lens wear, and superficial keratectomy. Limbal stem cell transplantation may be performed for more severe cases of LSCD. The goal of this surgery is to replenish the limbal stem cell compartment so that the diseased corneal epithelium can regenerate with normal corneal epithelium.

Contraindication

Limbal stem cell transplantation is contraindicated in the presence of significant active inflammation. This also includes severe dry eye disease (Dua et al. 2010).

Techniques and Principle Outcome

CLAU is performed preferentially for unilateral cases of LSCD. Autografts have the advantage of not requiring treatment with immunosuppression. The procedure involves excision of a conjunctival and peripheral corneal explant from the normal fellow eye. Typically, two clocks hours of tissue superiorly and inferiorly are removed. The graft usually includes 3 mm of conjunctiva and 1 mm of peripheral cornea. In the recipient bed, fibrovascular pannus, conjunctiva, and corneal epithelium are removed. The explants are sutured in corresponding positions superiorly and inferiorly in the recipient bed with 10-0 nylon (Liang et al. 2009; Dua et al. 2010).

Keratolimbal allografts are performed in bilateral LSCD and can be obtained either from cadaveric eyes or from living related donors. The transplantation of allografts from living related donors is procedurally similar to limbal autografting. In contrast, cadaveric allografts can be harvested from either whole globes or corneal scleral discs and involve transplantation of a 360° sclerocorneal ring graft. The ring explant can either be secured to the recipient limbus as a ring, or the ring can be partitioned into sections. The sclerocorneal ring is sutured to the host bed using 10-0 nylon. Allografts from a cadaveric source have the advantage over living related donor grafts of providing a 360-degree supply of limbal stem cells (Dua et al. 2010).

Amniotic membrane can be used in conjunction with both autografts and allografts. The amniotic membrane both has a barrier function and promotes the expansion of host-derived residual limbal stem cells (Dua et al. 2010).

In the initial 2 years following transplantation, the success rate of both limbal autografts and allografts are comparable. However after 2 years, the success rate of limbal allografts is less than the success rate of autografts dropping to less than 60% for allografts. The higher failure rate may be due to allograft rejection, despite the use of

systemic immunosuppressive therapy (Liang et al. 2009). Notably, living related donor allografts have a lower rate of failure compared to cadaveric allografts. This may be due to the explants from living related donors being "fresh" and HLA matched (Dua et al. 2010).

Other factors associated with graft failure include lid malposition, severe dry eye, and chronic inflammation. An improved ocular surface prior to grafting leads to a higher rate of graft survival. Ideally, eyelid abnormalities contributing to ocular surface disease should be addressed prior to limbal stem cell transplantation (Dua et al. 2010).

An improvement in visual acuity may not be seen postoperatively, and penetrating keratoplasty (PKP) may be required to restore vision. Indeed, patient should be counseled preoperatively that the objective of this surgery is not vision improvement, but both symptomatic improvement and restoration of corneal epithelial health. When a PKP is required, this should be done as a two-stage procedure with the limbal cell transplantation first and PKP second, in order to maximize the survival of the PKP graft (Liang et al. 2009; Dua et al. 2010).

Complications

CLAU carries the small risk of the contralateral donor eye developing LSCD. This risk also applies to living related donors. In order to mitigate this risk, smaller-sized grafts are used. Patients with either cadaveric or living related donor allografts need long-term immunosuppressive therapy and are thus at risk of incurring complications secondary to the use of immunosuppressives.

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Limbal Dermoid

▶ Epibulbar Tumor

Limbal or Epibulbar Dermoid

▶ Choristomas

Limbal Relaxing Incisions

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Synonyms

Peripheral corneal relaxing incisions

Definition

Limbal relaxing incisions are a refractive surgical procedure to correct astigmatism, most commonly during phacoemulsification. The procedure consists of making a pair of incisions at the limbus which have the effect of changing corneal astigmatism.

Epidemiology

Due to the fact that cataract surgery is one of the most highly frequented surgical procedures

worldwide, the number of limbal relaxing incisions is very high.

History

Starting in the 1990s, limbal relaxing incisions became popular for correcting corneal astigmatism of 0.5–4.0D. The technique was introduced by JP Gills, who also made nomograms to determine the length, number, and depth of the incisions.

Clinical Features

According to the Gills and Gayton nomograms which determine the length, number, and depth of incisions, generally a 6 mm incision corrects up to 2D of astigmatism. Paired incisions can correct up to 4D.

Tests

Thorough examination of the eyes and keratometric and keratographic readings are required for preoperative planning to assure the best possible correction of astigmatism.

Differential Diagnosis

Other corneal incisional surgeries are:

- Radial keratotomy
- Astigmatic keratotomy

Etiology

See History section above.

Treatment

After fixing the eye, the incision is made with the diamond blade just inside the conjunctiva. The blade should be oriented perpendicular to the surface of the cornea. This procedure should be done at the beginning of surgery to assure achieving a consistent incision depth and consistent intraocular pressure.

Cross-References

- ▶ Astigmatic Keratotomy
- ▶ Corneal Astigmatism
- ▶ Radial Keratotomy

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Limbal Stem Cell Transplantation

▶ Limbal Transplantation for Chemical Injury

Limbal Stem Cells

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Synonyms

LESCs: limbal epithelial stem cells

Definition

Adult cells located in the corneoscleral junction which have the ability to self-renew and repopulate the cells of the corneal epithelium.

Structure

The limbus is located between the clear cornea and the "white" of the sclera and clear conjunctiva. Limbal stem cells are located in special niches which regulate the microenvironment of the LSCs allowing them to remain in an undifferentiated state by providing appropriate growth factors. This niche, also known as palisades of Vogt, is a radially oriented ridge that harbors epithelial stem cells in deep epithelial ingrowths into the limbal stroma. As these stem cells proliferate, they migrate centripetally to ensure a corneal surface with a uniformly arranged epithelium.

Several structural differences exist between limbal epithelial stem cells and regular corneal epithelial cells. The LESCs containing palisades of Vogt are located at the highly pigmented superior and inferior limbus. The presence of the surrounding melanocytes at a unique location that is beneath the upper and lower eyelids provides these stem cells with an additional protection from UV radiation-induced DNA damage and mechanical injury.

The basement membrane of the limbal epithelium differs from that of the cornea in that it is undulated with papillae of the stroma that extend upward creating limbal crypts in between projections. LSCs interact closely with the underlying limbal stroma which increases its surface area. The proximity of the palisades of Vogt to the stromal vasculature enables the infiltration of necessary growth factors, antigen-presenting Langerhans cells, and suppressor T lymphocytes. The BM of the limbus is also unique in its preferential expression of alpha9 integrin and N-cadherin without Cx43. The limbal BM also contains laminin-1 and laminin-5 and a2b2 chains which are not present in the corneal basement membrane further emphasizing the unique niche which allows for limbal stem cells to function.

Although the concept of the limbal stem cell niche is well discussed, a recently published animal study in 2008 has proposed a mix of cells called compound niches. These compound niches consist of cells in different states of differentiation: corneal progenitors, mucin-producing goblet cells, and both proliferating and nonproliferating cells. Similar to the LESC niche, compound niches are thought to be at the limbus and migrate to areas of damaged corneal epithelium. This study also suggests that corneal epithelial progenitors are oligopotent; thus they can give rise to goblet cells in addition to corneal epithelial cells. This study provides an alternative to the existing body of knowledge of limbal stem cells and calls upon further research to clarify this concept in human and animal subjects.

Function

The function of the corneal limbus is bifold; it not only serves as a reservoir for the stem cells involved in the active renewal of the corneal epithelium, but it also serves as a barrier to conjunctivalization of the cornea. Essentially, limbal stem cells are the ultimate source of regeneration for the entire corneal epithelium which is necessary after the sloughing of dead epithelial cells with every blink of the eye or even after corneal epithelial injury. Consequently, when this limbal epithelial regenerative function fails, conjunctival epithelial cells with goblet cells replace the corneal epithelium, and a clear barrier to the eye is opacified by the growth of a vascularized conjunctiva due to chronic inflammation. This often culminates in visual impairment and chronic pain in those afflicted.

Clinical Relevance

Patients afflicted with limbal stem cell deficiency suffer from recurrent epithelial defects as the corneal epithelium is unable to regenerate; persistent pain from continuous breakdown of the ocular surface with concurrent inflammation ensues. This process may ultimately lead to a complete blindness in the affected eye.

Limbal stem cell deficiency can occur due to chemical burns of the eye (alkali and acid),

thermal burns, contact lens usage, or even topically administered drugs. Injury may be acquired if a therapy such as cryotherapy damages the LSCs along with their niche. Systemic diseases such as Stevens-Johnson syndrome and cicatricial pemphigoid can also produce patients with limbal stem cell deficiency.

The management of limbal stem cell deficiency can be medical or surgical. Medical management aims to lessen the symptoms of pain and the inflammation that often occurs with limbal stem cell deficiency. The use of topical lubricants, corticosteroids, and autologous serum drops are well documented as they stimulate corneal healing.

In contrast, the surgical options intend to cure the disease process. It is important to assess whether the patient produces an appropriate tear film and that the patient can completely close his or her eye. These will be important prerequisite for the surgery in order to maintain the corneal epithelium post-corrective surgery. The first step of the surgical procedure is to remove the scarred tissue from the cornea. This tissue is conjunctivalized due to the limbal stem cell deficiency. When the disease is unilateral, limbal tissue from the same patient's healthy eye may be used for autologous transplantation. If bilateral disease exists, then a living related donor or cadaver's limbal stem cells may be used for allogenic transplantation. Of these two methods, autologous transplantation is the preferred method, although the condition is that the other eye must have viable limbal stem cells which can be used.

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Limbal Transplantation for Chemical Injury

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Synonyms

Limbal stem cell transplantation

Definition

Limbal transplantation refers to the surgical procedure in which one takes autogenic or allogenic stem cells located at the periphery of the cornea (the limbus) and seeds these stem cells on the corneal surface of an eye lacking functioning limbal stem cells.

In the past few decades, several new surgical techniques have emerged which have significantly changed the prognosis of previously debilitating disease due to limbal stem cell dysfunction. In 2008, the Cornea Society's International Committee for the Classification of Ocular Surface Rehabilitation Procedures created a system such that surgeons may classify limbal transplantation procedures based on various divisions. With the advent of ex vivo cultivation of limbal stem cells, it is first important to classify whether this method was used or a simple explant/implant procedure was observed. Secondly, one must address the anatomical source of the tissue and whether the donor is an autograft or allograft. Autograft tissue will include limbal stem cells from an individual's non-diseased eye. Allograft tissue, however, can be further classified into living relative or cadaveric tissue. The following chart will help delineate the aforementioned classification system.

Limbal transplantation		Ex vivo cultivated limbal transplantation	
Procedure	Transplanted tissue	Procedure	Transplanted tissue
Conjunctival limbal autograft	Conjunctival limbus	Ex vivo cultivated cadaveric limbal autograft	Corneal limbus
Cadaveric conjunctival limbal allograft	Conjunctival limbus	Ex vivo cultivated cadaveric limbal allograft	Corneal limbus
Living related conjunctival limbal allograft	Conjunctival limbus	Ex vivo cultivated living related limbal allograft	Corneal limbus
Living non-related conjunctival limbal allograft	Conjunctival limbus	Ex vivo cultivated living non-related limbal allograft	Corneal limbus
Keratolimbal autograft	Corneal limbus		
Keratolimbal allograft	Corneal limbus		

Indication

A lack of functioning limbal stem cells is the sole indication for limbal stem cell transplantation. Conjunctival limbal autograft is the procedure of choice for unilateral stem cell deficiency and unilateral ocular surface injury (traumatic and chemical injury) with an unaffected eye. Living related conjunctival limbal allograft is indicated in patients with bilateral stem cell failure who have conjunctival loss in addition to their stem cell dysfunction: Stevens-Johnson syndrome, ocular cicatricial pemphigoid, and atopic keratoconjunctivitis. Keratolimbal allografts are indicated in the eyes with severe bilateral stem cell deficiency which require large amounts of cadaveric stem cells; it is also indicated in individuals with unilateral disease who fear damage to healthy fellow eye and have no living donor tissue available. Keratolimbal allografts are also good for disease that primarily affects the limbus with minimal conjunctival involvement, such as chemical injury (Stevens-Johnson syndrome and ocular cicatricial pemphigoid if inflammation is controlled beforehand). Ex vivo cultivated limbal transplantation is indicated when there is the need to transplant a large amount of limbal stem cell tissue while harvesting only a small amount. This is most important in autografts who do not want to risk the healthy fellow eye by depleted stem cell reserves which often result in deficiency after the donation.

Contraindication

Conjunctival limbal autografts are contraindicated if the donor eye has any condition that may predispose it to the development of stem cell deficiency: long-term topical medication use or contact lens wear, previous surgery, and uncontrolled inflammation. Cadaveric conjunctival limbal allografts are contraindicated in systemic disease which prevents the use of oral and topical immunosuppression, severe dry eye, and keratinization of the ocular surface. Living related conjunctival limbal allografts are contraindicated in patients with complete stem cell loss; partial stem cell dysfunctions are better candidates than those with complete loss because the amount of limbus that can be transplanted in this procedure is limited compared to keratolimbal transplants. Systemic disease which prevents the use of oral and topical immunosuppression is another contraindication alongside severe dry eye and keratinization of the ocular surface. Living related conjunctival limbal allografts are contraindicated in systemic disease which prevents the use of oral and topical immunosuppression. Keratolimbal allografts are contraindicated in cases where severe stem cell deficiency is present in combination with conjunctival inflammation, scarring, and keratinization. Lack of stable tear film, eyelid abnormalities, uncontrolled inflammation, and systemic disease which prevents the use of oral

and topical immunosuppression are relative contraindications.

Techniques and Principles

Several techniques exist for limbal transplants. Conjunctival limbal autografts (CLAUs) are begun by first performing a conjunctival peritotomy and removing the corneal epithelium. Next, the conjunctiva is recessed posteriorly, and the abnormal fibrovascular epithelium is removed by a superficial keratectomy. Two donor limbal grafts are then delineated at 6 and 12 o'clock areas of the donor limbus. After separating the conjunctiva from Tenon's capsule, the graft is dissected toward the cornea transecting the palisades of Vogt. The proximal margin of this donor tissue is then transected and transferred to the recipient eye. When suturing the graft to the corresponding area of the recipient eye, care must be taken to avoid placing sutures through the limbal margin in order to minimize stem cell damage. This same procedure would be followed for a cadaveric conjunctival limbal allograft (CLAL). A living related CLAL is done in two separate operations. First, the allograft is harvested from the donor as described for the CLAU procedure. While the tissue is immersed in colloidal storage solution, it is of utmost importance to correctly orient the graft while being stored. This is usually done with asymmetric marking of the graft with a gentian violet marker. After the recipient eye is prepared to receive the graft, the graft is sutured into place as done in the CLAU procedure.

A less common type of limbal transplant is the keratolimbal allograft (KLAL). This procedure has the addition of a corneoscleral rim used in the transplant process.

Ex vivo cultivated limbal transplantation is yet another option for limbal stem cell transplantation. The technique and principles are similar for each of these allografts, whether they be cadaveric, living related, or living non-related ex vivo cultivated limbal allografts. First, a small number of stem cells are harvested. Next, they are then allowed to proliferate in favorable growth factors and culture environment on a carrier material such as an amniotic membrane. The rest of the transplantation procedure is similar for all the techniques. A 360° peritotomy is then done with recession of the conjunctiva and Tenon's capsule. Abnormal corneal epithelium and fibrotic tissue are removed with a full superficial keratectomy. The graft is then placed on the now denuded cornea and sutured into place, and a therapeutic soft contact lens is placed overlying the graft.

Outcome

Outcomes are better with autografts as there is less risk for rejection. There are continuing improvements with concurrent immunosuppressive therapy.

Complications

A major complication of living limbal stem cell donors' eyes is the development of stem cell deficiency in that very donor eye. When any allogenic limbal stem cell source is used for transplantation, there is a significant risk of rejection; oral and topical immunosuppressives are often used for long periods.

Cross-References

► Limbal Stem Cells

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Limbal Vernal Conjunctivitis

► Limbal Vernal Conjunctivitis/Keratoconjunctivitis

Limbal Vernal Conjunctivitis/ Keratoconjunctivitis

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Synonyms

Limbal vernal conjunctivitis; Limbal Vernal Keratoconjunctivitis

Definition

Limbal Vernal Keratoconjunctivitis is an atopic disease whereby an allergic response is triggered by common environmental allergens such as pollen or dust resulting in a chronic papillary conjunctivitis. As noted by the term vernal, meaning springtime, Limbal Vernal Keratoconjunctivitis tends to be a recurring, seasonal inflammation of the conjunctiva and cornea.

Etiology

The genetic causes of Vernal Keratoconjunctivitis have not been fully determined. However, it is known that the atopy found in the Vernal Keratoconjunctivitis is driven by an overpopulation of Th2 T helper lymphocytes. These cells drive the disease process by a type 1, IgE-medicated hypersensitivity reaction. These Th2 lymphocytes produce interleukins 3, 4, and 13 which promote the synthesis of IgE by B lymphocytes. The papillae formed in Vernal Keratoconjunctivitis are formed by central vascular cores surrounded by edematous connective tissue.

Clinical Presentation

Patients with Vernal Keratoconjunctivitis present with symptoms of mucous discharge, itchy eyes, photophobia, blurred vision, and blepharospasm. Patients may have eczematous skin at the eyelids, with excoriations at the canthi. Papillary hypertrophy overlying the upper tarsal plates may result in giant papillae, greater than 1 mm in diameter. These giant papillae can give a cobblestone appearance. Depending where these giant papillae form, Vernal Keratoconjunctivitis can be classified as limbal, palpebral, or combined disease. Gelatinous collections of deposited eosinophils and epithelial cells can also form at the corneal limbus creating white Horner-Trantas dots.

Corneal changes can occur in the case of mild disease with punctate epithelial erosions, whereas with more intense palpebral involvement, mucus can be build up on the cornea resulting in corneal neovascularization. In severe palpebral disease, the release of toxic substances such as major basic protein from eosinophils can result in corneal epithelial macroerosions. If these erosions are not treated early and allowed to heal, then calcium deposition on Bowman's layer can prevent reepithelialization resulting in a shield ulcer or vernal plaque. Without proper healing, these erosions can be sources of infection such as herpes simplex keratitis or other complications. For example, up to 26% of patients have been found to develop keratoconus.

Diagnosis

Patients with Vernal Keratoconjunctivitis are diagnosed clinically based on presentation of signs and symptoms consistent with the disease as described above. Further investigations or tests to diagnose Vernal Keratoconjunctivitis are not widely available. Allergy testing is not indicated in the majority of these patients.

Differential Diagnosis

The differential diagnoses for Vernal Keratoconjunctivitis include other chronic papillary conjunctivitis, most predominantly Atopic Keratoconjunctivitis. Atopic Keratoconjunctivitis tends to be much less seasonal in nature and does not have an expected outcome resolving on its own after a few years.

Prophylaxis

Patients with mild to moderate disease that is seasonal in nature may attempt to prophylactically treat the disease by starting mast cell stabilizer drops at least 2 weeks prior to when symptoms generally begin. Patients with year-round disease may keep on year-round mast cell stabilizing topical medications.

Therapy

Therapy for this disease is determined based upon the severity of the disease. Mild cases may be treated with simply topical antihistamines. Topical H1 antagonists usually produce relatively quick relief of symptoms. Topical mast cell stabilizers can be used prophylactically for treatment. Combination of H1 antagonists and mast cell stabilizers include olopatadine 0.1%. These medications are safe for long-term use in patients.

Topical acetylcysteine has also been used to decrease mucus adherence to the cornea during episodes of Vernal Keratoconjunctivitis. More severe cases may require topical steroid or even topical immunomodulators such as cyclosporine. Topical steroids are most commonly used every 2 h for 5–7 days. Steroid-related complications can be avoided by using steroids for exacerbations instead of chronic treatment. Interestingly, the precipitation of particulate matter between papillae with prednisolone acetate can be avoided by using dexamethasone phosphate as the preferred steroid for topical treatment.

An alternative steroid treatment is the supratarsal subconjunctival injection of a steroid. However, the patient would have to be monitored for steroid-induced pressure spikes while receiving this treatment. In refractory cases of Vernal Keratoconjunctivitis, topical cyclosporine can also be administered two to four times a day.

Prognosis

The prognosis for Vernal Keratoconjunctivitis is generally positive. Unlike Atopic Keratoconjunctivitis, which presents later in life and tends to be a much more chronic, year-round disease, Vernal Keratoconjunctivitis more commonly presents during the first decade in life and usually resolves by the time the patient reaches his late teens.

Epidemiology

Vernal Keratoconjunctivitis typically develops by age 10 with a mean age of onset by 7 years old. In 95% of cases, the disease subsides by late adolescence.

Vernal Keratoconjunctivitis is more commonly found in young males, but this gender difference is less significant in the tropics. Although 3–10% of children in Africa and the Middle East are estimated to have Vernal Keratoconjunctivitis, the prevalence in children in Western Europe is only 0.03%. Limbal Vernal Keratoconjunctivitis is more common in Asian and African patients, and this difference in prevalence has been noted to remain even after migration to temperate regions.

Cross-References

- ▶ Allergic Conjunctivitis
- ▶ Conjunctivitis
- ▶ Horner-Trantas Dots
- ▶ Keratoconjunctivitis: Overview
- ▶ Palpebral Vernal Conjunctivitis/Keratoconjunctivitis
- ▶ Vernal Conjunctivitis/Keratoconjunctivitis

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Limbal Vernal Keratoconjunctivitis

► Limbal Vernal Conjunctivitis/Keratoconjunctivitis

Lindau Disease or Retinocerebellar Angiomatosis

► Hemangioblastomas, with Retinal Angiomatosis (von Hippel Lindau Disease)
► Retinae (Retinal Angiomatosis, von Hippel Syndrome/Disease)
► VHL Syndrome

Lipemia Retinalis

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Definition

Lipemia retinalis is characterized by creamy-white-colored retinal blood vessels in patients with hypertriglyceridemia.

Etiology

The scattering of light by high levels of triglyceride-laden chylomicrons in the plasma accounts for the fundus appearance.

Clinical Presentation

Lipemia retinalis is seen in some hyperlipidemic states (elevated serum triglyceride levels). There may be recurrent abdominal pain due to pancreatitis and/or eruptive xanthomas associated with chylomicronemia. There are no changes in visual acuity, but fundus changes include whitish retinal vessels and a salmon-pink retina (Kanski et al. 2011). Elevated plasma triglyceride levels may have other ocular manifestations (e.g., lipemic aqueous, corneal arcus, xanthelasma, palpebral xanthomas, retinal vein sludging, red cell aggregation).

Diagnosis

A blood test should be performed to detect hyperlipidemia. Fundus examination can reveal:

- Early stage (triglyceride levels 2,500–3,499 mg/dL): creamy and thin peripheral vessels
- Moderate stage (triglyceride levels 3,500–5,000 mg/dL): creamy posterior pole vessels
- Late stage (triglyceride levels >5,000 mg/dL): salmon-colored fundus, creamy vessels

Electroretinogram amplitude may be decreased.

Differential Diagnosis

– Hypertriglyceridemia ± chylomicronemia syndrome
  Primary familial lipid disorder (hyperlipoproteinemia types I, III, IV, or V)

Secondary hyperlipidemia: diabetes mellitus, biliary obstruction, nephrotic syndrome, pancreatitis, hypothyroidism, alcoholism, medications (estrogens, beta-blockers, protease inhibitors), and acquired immunodeficiency syndrome

Prophylaxis

Regular physical activity with a low-fat diet.

Therapy

Treatment is necessary for the systemic effects of hypertriglyceridemia, but no treatment is required for the lipemia retinalis itself. A low-fat diet alone is often sufficient to reverse ocular findings. Medium-chain fatty acids (including medium-chain triglyceride milk for neonates) can provide a source of fat in the diet because they do not rely on chylomicron formation (Zahavi et al. 2013).

Prognosis

Lipemia retinalis quickly improves (within 1 week) as triglyceride levels return to normal.

Epidemiology

Lipemia retinalis is a rare condition that may occur in neonates and children as a result of a primary familial lipid disorder (e.g., ApoC-II deficiency, LPL deficiency) or in adults secondary to other diseases (Hoyt et al. 2013).

Cross-References

- ▶ Corneal arcus
- ▶ Xanthelasma
- ▶ Xanthomas

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Lipid Keratopathy

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Synonyms

Corneal lipid degeneration

Definition

Lipid keratopathy is pathology of the cornea that leads to decreased vision due to intracellular and extracellular corneal lipid deposits and/or neovascularization. Primary lipid keratopathy is often bilateral, hereditary, avascular, and in the absence of any underlying condition. Secondary lipid keratopathy is unilateral, peripheral, non-hereditary, vascular, and associated with an underlying condition.

Etiology

The etiology of lipid keratopathy depends on whether the disease is primary or secondary. Primary lipid keratopathy is a rare disease and has features of a corneal dystrophy. Secondary lipid keratopathy, in contrast, has features characteristic of degeneration. The other major difference is that primary lipid keratopathy has no underlying metabolic disorder, while secondary lipid keratopathy is often linked to an underlying systemic disease.

The deposits of both are formed from triglycerides, cholesterol, and phospholipids (Chang and Ching 2011).

As previously mentioned, primary lipid keratopathy has no underlying disorder of lipid metabolism. In fact, the lipid levels are often normal (Chang and Ching 2011). There is some question as to whether or not primary lipid keratopathy may be an advanced arcus senilis. Both arcus senilis and lipid keratopathy deposit lipids in the posterior stroma and Descemet's membrane (Chang and Ching 2011). It is hypothesized that the lipid deposits are due to increased limbal vessel permeability and the release of fatty products into the stroma as keratocytes die (Chang and Ching 2011).

Secondary lipid keratopathy often occurs very suddenly. Neovascularization is present in secondary lipid keratopathy, and these vessels are more permeable and clear lipids less effectively. This is why when lipid levels in the body rise, progression of the gray/yellow infiltrate can occur (Chang and Ching 2011). When the individual's lipid levels return to normolipoproteinemia, there is an associated regression of the infiltrate (Chang and Ching 2011). Secondary lipid keratopathies are often the result of aging, environmental stimulus, or inflammation (Kanski and Bowling 2011). The most common cause of secondary lipid keratopathy is herpes simplex and herpes zoster (Kenyon et al. 2008). Lipid keratopathy can also be seen with interstitial keratitis, corneal hydrops, trauma, ulceration, and mustard gas injury (Chang and Ching 2011). Some can be inherited dystrophies that deposit lipid and include Tangier disease, apolipoprotein A-1 deficiency, lecithin cholesterol acetyltransferase (LCAT) deficiency, and fish-eye disease (Chang and Ching 2011; Woodward et al. 2014).

There are a few options in treating the symptom of lipid keratopathy. While achieving normolipoproteinemia is associated with regression of secondary lipid keratopathy, there are other options if blood lipid levels are inadequate. Argon laser can be used to induce lipid resorption, or needlepoint cautery can be used to target the feeder vessels (Kenyon et al. 2008). In advanced disease, penetrating keratoplasty can also be used (Kenyon et al. 2008; Chang and Ching 2011). Treatment is often very successful, but recurrence of primary lipid keratopathy has been documented in case reports (Chang and Ching 2011).

Occurrence

Primary lipid keratopathy is a rare disease and shows features of a dystrophy. Dystrophies occur bilaterally and are hereditary. When primary lipid keratopathy occurs, they are bilateral, non-inflammatory, avascular deposits of white/yellow lipid in the central cornea (Kenyon et al. 2008; Chang and Ching 2011; Kanski and Bowling 2011). These dystrophies occur early in life, as compared to degenerations, which often are considered aging effects and occur later in life.

Secondary lipid keratopathy shows features of a degeneration. Degenerations begin with normal function and over time deteriorate in function. Unlike primary lipid keratopathy, the lipid deposits are often unilateral. Also, unlike primary lipid keratopathy, the lipid deposits occur more peripherally, but can also progress to involve the central cornea (Kanski and Bowling 2011). The deposits can either be feathery in post-inflammatory states or discoid when occurring in active inflammation (Chang and Ching 2011).

Lipid keratopathy is more common in women, with a ratio of 70:30. While it is not well understood, it is hypothesized that the higher levels of HDL cholesterol in premenopausal women contributes to this higher prevalence (Chang and Ching 2011).

Classification

Lipid keratopathy is classified either as primary or secondary. These differ in their etiology and

occurrence with the distinctions as discussed above.

Cross-References

- ▶ Herpes Simplex Virus
- ▶ Herpes Zoster
- ▶ Herpes Zoster Ophthalmicus
- ▶ Interstitial Keratitis
- ▶ Tangier Disease, Corneal Changes

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Liposomal Amphotericin B (L-AmB)

- ▶ Amphotericin B, for *Aspergillus* Endophthalmitis

Lisch Corneal Dystrophy

- ▶ Corneal Dystrophies

Lisch Epithelial Corneal Dystrophy

- ▶ Epithelial Dystrophies

Lisch Nodules, in Neurofibromatosis

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Synonyms

Sakurai-Lisch nodules

Definition

Lisch nodules are smooth, dome-shaped, pigmented hamartomas of the iris.

Basic Characteristics

Lisch nodules are commonly found in patients with neurofibromatosis type 1 (NF1) but are not a diagnostic feature of neurofibromatosis type 2. Lisch nodules are not generally present at birth but develop over time in 94–97% of patients with NF1 who are over the age of 6 and in essentially all patients with NF1 by the age of 30. Lisch

nodules can be translucent, tan, or brown and are usually more prevalent on the inferior iris. They are bilateral, elevated, and often gelatinous and typically measure between 0.5 and 1.0 mm in diameter. Lisch nodules are asymptomatic but can be helpful in the diagnosis of NF1, especially when discovered in asymptomatic relatives. The diagnosis of NF1 is made when a patient has at least two of seven established findings, one of which is multiple Lisch nodules.

Further Reading

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Lithiasis, Conjunctival

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Synonyms

Conjunctival concretions

Definition

Conjunctival lithiasis refers to the small, hardened superficial subepithelial deposits that occur as a result of secondary calcification of conjunctival concretions. Though the two terms are often used synonymously, histopathological evidence has revealed that concretions do not routinely contain calcium or phosphate but are composed of products of cellular degeneration including epithelial and keratin debris. Lithiasis may lead to irritation due to mechanical microtrauma of the corneal epithelium, in which case they can be removed at the slit lamp under topical anesthesia.

Cross-References

▶ Concretions, Conjunctival

Little Old Adie's Pupil

▶ Anisocoria: Big Pupil
▶ Tonic Pupil (Adie's Pupil), Pharmacological Testing for

Liver Spots

▶ Lentigo Senile (Liver Spots)

LMBBS

▶ Bardet–Biedl Syndrome, Renal

LMS

▶ Bardet–Biedl Syndrome, Renal

Lobar Capillary Hemangioma

▶ Pyogenic Granuloma

Local Advancement Flap

▶ Semicircular Flap for Eyelid Repair
▶ Tenzel Flaps
▶ Transposition Flaps, for Lateral Canthal Defects

Local Anesthesia for Ophthalmic Procedures

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Synonyms

Regional anesthesia

Definition

(Local) regional anesthesia for ophthalmic procedures refers to the administration of anesthetic agents either topically, intraocularly, or by injection. The route of administration depends on several factors, including surgeon and patient preference, patient's ability to follow commands, type and length of procedure, and amount of akinesia required. Topical anesthesia allows for anesthesia of the conjunctiva, cornea, and anterior sclera. Intraocular anesthesia may be used as an adjunct to topical anesthesia to achieve anesthesia for the intraocular structures, such as the iris, as well as to reduce the sensation of pressure fluctuations in the anterior chamber. Injection anesthesia can be delivered by parabulbar (subtenon's), peribulbar, or retrobulbar routes and provides anesthesia to the ocular surface and intraocular structures. Injection anesthesia also allows for a decrease or elimination of the extraocular movements.

Cross-References

► Anesthesia (Anesthetics), Local

Localized Corneal Amyloidosis

► Lattice Lines

Longitudinal Chromatic Aberration

► Chromatic Aberration: Definition

Longsightedness

► Hyperopia

Louis-Bar Syndrome

► Ataxia-Telangiectasia (A-T)

Lower Lid Retraction

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Definition

Eyelid retraction is the displacement of the normal position of the lower eyelid margin with respect to the limbus.

Basic Characteristics

Clinical Features

In most normal individuals, the lower eyelid margin rests at the level of the inferior limbus. In lower lid retraction, the eyelid position is depressed below this level, producing inferior scleral show. Eyelid retraction may be unilateral or bilateral. Mild retraction of the eyelids may occur as a normal anatomical variant of eyelid position seen in patients with axial myopia, shallow orbits, maxillary hypoplasia, or certain genetic orbital or eyelid characteristics. Involutional changes with laxity of the tarsal canthal tendons may also manifest as lower lid retraction.

Lid retraction can lead to lagophthalmos and corneal exposure, leading to secondary epiphora and dry eye symptoms.

Diagnostics

Position of lower eyelid with relation to limbus, height of the palpebral fissure, degree of lagophthalmos, associated proptosis, levator muscle function, distance from lower eyelid margin to the central corneal reflex, and radiological studies.

Etiology

The most common cause of lower eyelid retraction is Graves' disease. Although the exact mechanism of retraction associated with Graves' disease is debated, histopathologic changes include inflammation, adipogenesis, and fibrous contraction of eyelid retractors.

Other causes of lower lid retraction include postsurgical complications after vertical rectus muscle surgery, with anatomical connections between the inferior rectus and capsulopalpebral fascia. Lid malposition is also a well-known postoperative complication of lower lid blepharoplasty, occurring more frequently in patients with preexisting lid laxity and excessive skin resection at surgery.

Cross-References

- ▶ Graves' Disease
- ▶ Spasm of Eyelids
- ▶ Upper Lid Retraction

Further Reading

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Lues

▶ Syphilis: Overview

Lues Venerea

▶ Syphilis: Overview

Luminance: Definition

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Definition

Luminance is a photometric measure of luminous intensity L [$cd \cdot m^{-2}$]. In contrast to radiance or brightness, luminance defines the amount of light visually perceived by the eye accounting for the spectral sensitivity curve $V(\lambda)$. It is used to specify emission from flat, diffuse emitting/reflecting surfaces such as visual acuity test charts (e.g., 85 $cd \cdot m^{-2}$ for photopic ETDRS test). If the spectral distribution of a light source is known, luminance can be calculated from radiance L_e: $L = 683 \frac{lm}{W} \cdot \sum V(\lambda) \cdot L_e(\lambda)$. Luminance usually used for reporting visually perceived intensity of light sources or displays.

Cross-References

- ▶ Candle Power (Luminous Intensity)
- ▶ ETDRS Visual Acuity Chart

- ▶ Photoreceptor Cells
- ▶ Radiance

Lutein

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Synonyms

Macular xanthophyll

Definition

Lutein is one of the hundreds of carotenoids found in nature. Carotenoids are lipophilic pigments that absorb light, creating the different colors. Lutein belongs to a subclass of carotenoids called xanthophylls. Xanthophylls have unique biochemical properties due to a free hydroxyl groups at each end of the molecule, differentiating them from other carotenoids with similar structures. These hydroxyl groups allow for specific orientation within cell membranes and lipoproteins.

Lutein is one of the less than 20 carotenoids found in the human body. Carotenoids are not produced in the body and must be consumed through diet. Leafy green vegetables like spinach and kale and egg yolks, due to poultry-feed supplementation, are good sources of lutein.

Lutein and another xanthophyll, zeaxanthin, make up the macular pigment of the eye. Through their antioxidative properties, it is thought that lutein and zeaxanthin act to protect photoreceptors in the macula from potential free radical damage. Lutein and zeaxanthin may also act to filter high-energy blue light wavelengths, reducing the potential oxidative stress from light entering the eye. Lutein is also likely the precursor to meso-zeaxanthin, a third carotenoid found in macular pigment that has a very similar structure to lutein. Meso-zeaxanthin is not found in blood serum and is likely derived from lutein undergoing a photochemical transformation.

Indication

The anti-oxidative properties of lutein and other xanthophylls may be helpful in decreasing age-related changes like macular degeneration and cataract in the eye. In 1994, Seddon et al. showed a direct correlation between dietary intake of carotenoids and the reduced risk of exudative age-related macular degeneration. Report number 22 by the Age-Related Eye Disease Study (AREDS) Research Group also found that high dietary intake of lutein and zeaxanthin is independently associated with decreased likelihood of having extensive intermediate drusen, geographic atrophy, and neovascular age-related macular degeneration. The Carotenoids in the Age-Related Eye Disease Study (CAREDS) group have found that diets rich in lutein and zeaxanthin are also associated with decreased prevalence of nuclear cataract in older women. Dietary supplementation with lutein may prevent or delay the onset of age-related macular degeneration and cataract. A large multicenter trial, the age-related eye disease study II (AREDS 2), studying the effects of oral macular xanthophylls and/or omega-3 fatty acids for the treatment of age-related macular degeneration and cataract is currently underway.

Contraindication

Known sensitivity to lutein.

Use and Dosage

There is no recommended daily allowance (RDA) for lutein. The age-related eye disease study II

(AREDS 2), a large multicenter trial studying the effects of oral macular xanthophylls and/or omega-3 fatty acids for the treatment of age-related macular degeneration and cataract, is using a lutein/zeaxanthin tablet of 10 mg of lutein and 2 mg of zeaxanthin. Average daily intake of lutein/zeaxanthin is 3–4 mg.

Adverse Reactions

There are no known harmful side effects. Minor side effects such as difficulty in swallowing pills and headache have been reported.

Interactions

There are no known serious interactions reported with lutein.

Cross-References

- ▶ Age-related Macular Degeneration
- ▶ Carotenoids (Xanthophylls)
- ▶ Cataract, Causes and Treatment

Further Reading

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Luxated Lens

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Synonyms

Ectopia lentis; Lens instability, Lens luxation

Definition

Partial or total dislocation of the crystalline lens as a result of instability of the clamping system of the crystalline lens.

Histology

The ciliary body with its zonular fibers represents the fixture of the crystalline lens. Disturbances of this fixture can result in a luxation of the crystalline lens. Fifty percent of all cases of lens luxation are traumatic caused by boisterous beats or injuries. Other causes are genetic disorders accompanied with congenital weakness of connective tissues such as Marfan's syndrome, Marchesani's syndrome, and homocystinuria. Another pathomechanism of lens luxation can be a non-treated mature cataract. In this case, the crystalline becomes progressively thick and heavy. As a result the lens clamping system decompensates. Because of its anatomical position behind the iris,

a luxation backward into the vitreous body is more common than a luxation through the pupil into or the anterior chamber.

Immunohistochemistry

There are no data available in this topic.

Electron Microscopy

There are no data available in this topic.

Molecular Diagnostics

There are no data available in this topic.

Differential Diagnosis

Subluxated lens
Iris cyst
Lentodonesis
Iridodonesis

Cross-References

► Ciliary Body

Further Reading

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Lyme Borreliosis

► Lyme Disease

Lyme Disease

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Synonyms

Borrelia burgdorferi; Lyme borreliosis

Definition

Lyme disease is a tick-borne illness caused by the spirochete bacteria *Borrelia burgdorferi.* Its effects on the body are variable and wide ranging, including clinical manifestations in the skin, heart, nerves, and eyes. Ocular manifestations of Lyme disease include, but are not limited to, keratitis, follicular conjunctivitis, optic neuritis, and retinitis. These ocular findings occur throughout the course of the infection: either early on or during the later manifestations of disease. Ocular manifestations of Lyme disease are estimated to occur in up to 10% of patients with Lyme disease.

Etiology

The spirochete bacteria *Borrelia burgdorferi* is the causative agent in Lyme disease. The bacterium infects human hosts through a bite by the tick *Ixodes scapularis*. Once the bacterium is transmitted to the human host, it travels throughout the body, preferentially affecting tissues of the skin, joints, heart, and peripheral nerves. *Borrelia* is a highly motile bacterium. Its swift penetration through layers of tissue is attributed to its ability to bind host-derived plasmin on cell membranes, which then permits its entry into cells. *Borrelia* likely infects the eye through this mechanism. The most common ocular manifestations of Lyme disease, namely, keratitis and inflammation of the posterior chamber, are thought to occur as part of the generalized inflammation – arthritis, carditis, and peripheral neuritis – that presents a few weeks to months after initial infection. These manifestations occur if the initial presenting signs of infection, namely, the rash of erythema migrans, went undiagnosed and untreated.

Clinical Presentation

The clinical presentation of Lyme disease varies greatly and can have several different presenting signs and symptoms depending on how far away from initial infection the diagnosis is made. At the time of the acute infection, the characteristic rash of erythema migrans is typically visible. Generalized lymphadenopathy, headache, follicular conjunctivitis, and photophobia may follow. A few weeks to months after initial presentation, dissemination of the bacterium occurs and carditis (palpitations, arrhythmias, heart block, myocarditis), arthralgias, and facial nerve palsy all can occur. This is the stage at which the greatest variety of ocular manifestations can be observed. Nonstaining bilateral keratitis is the most common ocular presentation at this stage; however, iritis, uveitis, macular edema, optic disk edema, optic neuritis, and Horner's syndrome have all been described. At the third stage of infection, manifestations of disease are more chronic and include persistent arthritis – usually of large joints – fatigue, stromal keratitis, and episcleritis.

Diagnostics

If a patient presents early while the lesion of erythema migrans is still present, diagnosis based on this clinical criteria alone is sufficient. Serologic testing is likely to be negative this early on because the body has not had sufficient time to mount an immune response. Laboratory study confirmation of infection is needed to definitively establish a diagnosis of Lyme disease at later stages when the classic erythema migrans rash has usually disappeared. The most accurate laboratory test for Lyme disease involves culture and PCR amplification on a sample from the suspected site of infection. However, culture and PCR can only be done in very specialized laboratories, so antibody detection is currently the most common test used to diagnose Lyme borreliosis. A staged approach is typically used to establish diagnosis. First, a screening test such as an ELISA or immunofluorescent assay is performed. If this test is positive, a Western blot is performed to confirm diagnosis. Although ocular findings consistent with Lyme disease can be appreciated on slit lamp or fundoscopic exam, the clinical presentation can mirror many other diagnoses, hence serologic confirmation is necessary.

Differential Diagnosis

The manifestations of Lyme borreliosis, especially ocular Lyme, are very diverse. Therefore, there is a very broad differential diagnosis for each ocular manifestation. Lyme keratitis is probably the most common ocular manifestation. Since generalized inflammation is also present, other inflammatory syndromes that cause ocular findings, such as reactive arthritis, rheumatoid arthritis, and sarcoidosis, must all be considered. Staphylococcal keratitis, contact-lens-associated keratitis, and corneal abrasion are also all in the differential.

Prophylaxis

The best prophylaxis against Lyme disease is prevention of the tick bite by way of wearing long sleeves, DEET-containing insect repellent, and checking the body for ticks daily if someone is in an endemic area. If a person presents with a known tick bite, antibiotic prophylaxis against Lyme disease is not usually recommended unless certain parameters have been met. If the patient is being seen within 72 h of the tick bite, the tick looks like it has been attached for greater than 36 h, it can reliably be identified as an *Ixodes scapularis* tick, and the bite occurred in an area where greater than 20% carry *Borrelia*, 1 dose of 200 mg oral doxycycline has been shown to be very effective in preventing Lyme disease. Otherwise, the best prophylaxis for ocular Lyme borreliosis is early detection of infection and prompt treatment. If Lyme is diagnosed at the initial stage of cutaneous infection, many of the ocular sequelae can be prevented.

Therapy

If Lyme disease is diagnosed and treated early, 100 mg of oral doxycycline two times daily for 14 days is the recommended treatment in adults and nonpregnant, non-lactating women (oral amoxicillin 500 mg three times per day for 14 days is recommended in pregnant or lactating women). If the early conjunctivitis is present at this stage, no other direct ophthalmic treatment is recommended, as it should resolve with oral antibiotic therapy. If Lyme disease is diagnosed during the more advanced stages of disease, including the more severe ocular manifestations of keratitis, uveitis, and episcleritis, IV ceftriaxone for 14 days is typically used. This is the same treatment regimen that is used for late-presenting neurologic manifestations, such as meningitis, radiculopathies, or peripheral or cranial nerve palsies. Topical ophthalmic steroid solutions have occasionally been used in conjunction with the antibiotic regimen, but research is lacking in proving that their application truly speeds resolution of symptoms or prevents recurrence.

Prognosis

As is the case in many illnesses, prognosis is dependent on the stage of disease at which the diagnosis is made. On the whole, the earlier that ocular Lyme is diagnosed and treatment is started, the better the prognosis is. There are several case reports describing the relapsing remitting nature of Lyme-associated uveitis and episcleritis. In most of these cases, the recurrent inflammation was controlled with IV ceftriaxone and occasionally topical steroids. Vision is usually preserved. There are isolated cases of rapid deterioration of vision due to extensive inflammation of the posterior chamber and retinal detachment; however, these are very rare.

Epidemiology

There are varying reports of the prevalence of ocular Lyme disease. It is generally considered rare, especially the later sequelae of disease. However, there are reports describing that up to 10% of patients will have follicular conjunctivitis as part of the initial presentation of Lyme disease.

Cross-References

- ▶ Bacterial Conjunctivitis
- ▶ Bacterial Keratitis
- ▶ Follicular Conjunctivitis
- ▶ Uveitis in Multiple Sclerosis

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Lymphangiectasia

► Vascular Tumors Disease of the Conjunctiva

Lymphangioma

► Chocolate Cyst
► Vascular Tumors Disease of the Conjunctiva

Lymphoma: Definition

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Definition

A hematologic malignancy characterized by monoclonal, neoplastic proliferation of leukocytes of lymphoid origin that is capable of producing masses within the involved lymph nodes and/or in other tissues. The World Health Organization classification, last updated in 2008, divides lymphoma into three broad categories by cell types: B cell, T cell, and natural killer cell (Swerdlow and International Agency for Research on Cancer, World Health Organization 2008).

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Lynch Incision, for Anterior Orbitotomy

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Synonyms

Frontoethmoidal incision, for anterior orbitotomy

Definition

A transcutaneous orbitotomy designed to access the medial orbital wall and extraperiosteal space.

Indications

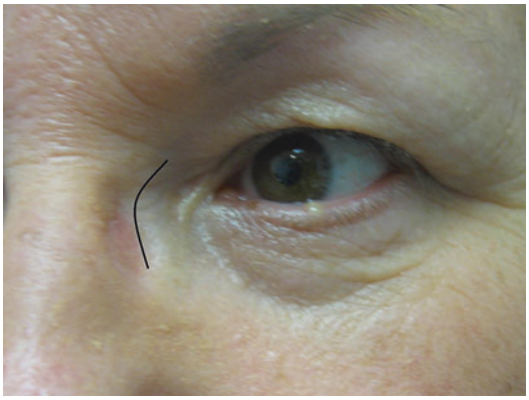
This procedure is used to access the medial wall when a transcaruncular approach does not offer enough exposure. It may be useful in treatment of posttraumatic telecanthus requiring fracture repair or transnasal wiring, or for other nasal fracture repair. It also may be used for drainage of a subperiosteal abscess, for orbital fracture repair, or for bony decompression of the medial orbit.

Contraindication

Contraindications for patients who wish to avoid a skin incision and for patients who are not medically stable for surgery.

Techniques and Principles

This area is approached with a curved skin incision placed approximately half way between the medial canthus and the bridge of the nose extending from the inferior to superior orbital rims as necessary (Fig. 1). Posterior dissection is that carried out to reach the medial orbit. At the end of the procedure, meticulous skin closure is performed in several layers to reduce the risk of scarring.



Lynch Incision, for Anterior Orbitotomy, Fig. 1 Medial canthal area of patient depicting skin marking generally used for lynch incision, showing a curvilinear incision half way between the medial canthus and the bridge of the nose

Outcome

Broad visualization of the subperiosteal spaces of the orbital wall for drainage of an abscess, bony decompression, or orbital or nasal fracture repair.

Complications

Risks include anesthesia, bleeding, pain, infection, scarring, swelling, loss of vision, damage to adjacent structures, diplopia, and need for additional procedures.

Cross-References

- ▶ Extraperiosteal Route
- ▶ Graves Ophthalmopathy
- ▶ Orbit, Inflammation of
- ▶ Orbitotomy
- ▶ Telecanthus
- ▶ Transcaruncular Route, for Anterior Orbitotomy

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Macroaneurysms

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History

Cases describing isolated retinal arteriole macroaneurysms have been described since the late 1880s. The term retinal arterial macroaneurysm (RAMA) was first coined by Dennis Robertson in 1973 (Robertson 1973).

Definition

Retinal macroaneurysms are acquired round or fusiform dilations of the retinal arterioles occurring in the first three bifurcations of the retinal arteriole (Robertson 1973).

Etiology

The etiology is unknown. Some consider the occurrence of the aneurysm to occur in association with arteriosclerosis, resulting in a decreased elasticity of the vessel wall and with increase in the luminal pressure that causes the dilation. Another hypothesis considers that emboli or thrombus formation causes damage to the vessel wall, which causes the outpouching (Palestine et al. 1982; Wiznia 1992; Gass 1997; Somnez et al. 2012).

Clinical Presentation

Macroaneurysms may occur in any quadrant; however, the superotemporal quadrant is the most commonly reported due to the visual impairment that occurs from lesions in that area. Retinal macroaneurysms may be asymptomatic and picked up only on routine evaluation or present with distortion or loss of vision if blood or serous detachment occurs in the fovea. Hemorrhage is often a presenting feature and may occur subretinal, intraretinal, subhyaloid (or preretinal), or into the vitreous or in an "hourglass" appearance with hemorrhage in multiple layers. They may be present on the optic nerve (Brown and Weinstock 1985) and cilioretinal artery (Giuffre et al. 1987) and may be pulsating.

Diagnostic Testing

The diagnosis is usually made clinically when one sees a small white outpouching associated with exudation or with an hourglass hemorrhage. The diagnosis can be confirmed by fluorescein angiography. If preretinal blood obscures the area of the aneurysm, indocyanine green angiography

U. Schmidt-Erfurth, T. Kohnen (eds.), *Encyclopedia of Ophthalmology*,
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can be utilized (Townsend-Pico et al. 2000). Blood pressure measurements and lipid profile are recommended.

Differential Diagnoses

Retinal capillary angioma, diabetic retinopathy, cavernous hemangioma, malignant melanoma (Fritsche et al. 2000), hemorrhagic pigment epithelial detachment associated with macular degeneration, Coats' disease, branch vein occlusion (Schulman et al. 1981; Cousins et al. 1990), retinal telangiectasis.

Therapy

Treatment remains controversial. Studies have shown the natural history can be very good. Many macroaneurysms do not leak into the fovea and can be observed; however, chronic leakage in the macula, if left untreated, may lead to permanent visual decrease. In one study, laser photocoagulation to the macroaneurysm was not found to be advantageous. Other studies, however, have shown visual improvement when laser photocoagulation is applied directly to the macroaneurysms and surrounding tissues. Light laser to the macroaneurysm has been recommended to avoid an arterial occlusion distal to the aneurysm. If bleeding occurs under the fovea, treatment to displace the blood may be indicated. Both pneumatic displacement and vitrectomy with subretinal TPA and gas have been described (Somnez et al. 2012). Recent articles have shown an improvement of vision with intravitreal bevacizumab injections (Cho et al. 2013; Zweifel et al. 2013). After macroaneurysms bleed, they usually go on to closing.

Epidemiology

The lesions are usually found in elderly woman (71–80%) with a history of hypertension or arteriolar sclerosis in the sixth decade of life. Macroaneurysms have been reported in younger patients, though rare. Macroaneurysms tend to be unilateral and single. Bilateral macroaneurysms may occur 10% of the time and multiple within the same eye 20% of the time. Macroaneurysms have associated with diabetes elevated lipids, retinal vasculitis (Kincaid and Schatz 1983), collagen vascular disease, and sarcoid though not consistently. Hypertension appears to be the most commonly associated systemic disease (Cleary et al. 1975; Lewis et al. 1976; Abdel-Khalek and Richardson 1986).

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Macropsia

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Synonyms

Megalopia

Definition

Macropsia is a disorder of visual perception in which a portion of the vision appears larger than normal. Compression of retinal photoreceptors can cause greater stimulation of retinal elements and the resulting perception of macropsia. Macropsia is a type of dysmetropsia (visual illusion).

Etiology

Macropsia usually results from retinal conditions (e.g., epiretinal membrane and macular edema) but can be due to cortical processing defects when bilateral or hemianopic.

Diagnostics

A complete eye exam and an Amsler grid can document the laterality, location, size, and severity of macropsia. A New Aniseikonia Test (NAT) can also be used to detect and quantify the degree of macropsia effect. Brain imaging or EEG may be necessary for patients with cortical macropsia especially if bilateral, simultaneous, or hemianopic.

Therapy

Treatment should be directed at the underlying etiology.

Cross-References

- ▶ Metamorphopsia
- ▶ Micropsia

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Macular Coloboma

► Ectasia, Retinal

Macular Corneal Dystrophy (MCD)

► Corneal Dystrophies

Macular Corneal Dystrophy (MCD), Groenouw Corneal Dystrophy Type II or Fehr Spotted Dystrophy

► Stromal Dystrophies

Macular Dystrophy

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Synonyms

Hereditary macular dystrophy; Inherited macular dystrophy

Definition

Macular dystrophy is a nonspecific term to describe a heterogeneous variety of inherited ocular disorders in which the posterior pole of the retina is predominantly affected. These disorders may present with characteristic macular abnormalities, decreased visual acuity, or both. Several gene mutations have been identified which result in macula involving changes in the eye, and it is anticipated that more will be identified in the future. The extent of visual acuity changes and macular findings is variable and dependent on the underlying disease, the extent of gene expression and penetration, and the stage of its progression.

Basic Characteristics

Macular findings with macular dystrophies are extremely variable and can range from very minimal to extensive changes. Different layers of the retina, retinal pigment epithelium (RPE), Bruch's membrane, or choriocapillaris may be the predominant site of involvement. Potential findings include cystic macular changes, drusen, vitelliform lesions or other deposits in the posterior pole, atrophic changes, bull's eyelike maculopathy, and pigmentary changes. A list of some macular dystrophies with an attempted classification based on area of involvement is shown below:

Macular dystrophies
Nerve fiber layer
- X-linked juvenile retinoschisis

Photoreceptor and RPE
- Cone (-rod) dystrophy
- Congenital color vision defects
- Best vitelliform dystrophy
- Stargardt's disease/fundus flavimaculatus
- Doyne's honeycomb retinal dystrophy/malattia leventinese
- Pattern dystrophy
- North Carolina macular dystrophy/central areolar pigment epithelial dystrophy
- Dominant cystoid macular dystrophy

Bruch's membrane
- Sorsby fundus dystrophy
- Angioid streaks – associated with several different systemic conditions
- Myopic degeneration

Choroid
- Central areolar choroidal dystrophy

Evaluation of patients with suspected macular dystrophy should include a detailed family, medical, and ocular history and a through ocular exam including color vision, dark adaptation, and Amsler grid testing. Ocular imaging that may be helpful includes visual field testing, fluorescein angiogram (FA), autofluorescence, and optical

coherence tomography (OCT). Electrophysiologic testing with both full-field and multifocal electroretinograms (ERGs) or electrooculograms (EOGs) may also aid in diagnosis. Genetic testing is available for a variety of macular dystrophies.

Cross-References

- ▶ Angioid Streaks
- ▶ Best Disease
- ▶ Color Blindness
- ▶ Cone Dystrophies/Degeneration
- ▶ Cone-Rod Degeneration
- ▶ Cone-Rod Dystrophy
- ▶ Doyne Honeycomb Degeneration of Retina
- ▶ Fundus Flavimaculatus (Stargardt Disease/Juvenile Macular Degeneration)

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Macular Edema

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Synonyms

Macular swelling; Macular thickening

Definition

Macular edema is an abnormal thickening of the neurosensory retina in the area of the macula with the intra- and/or extracellular accumulation of excess fluid. It represents a common final pathway of numerous retinal disorders, and it is the leading cause of central vision loss in the developed world. In most cases, it consists of a severe disturbance of the blood retina barrier. The diseases-causing macular edema is multiple and includes: choroidal neovascularization, diabetic retinopathy, retinal venous occlusion, postoperative cystoid macular edema, uveitis, tractional maculopathy, inherited retinal dystrophy, vascular and optic nerve abnormality, intraocular tumor, and idiopathic macular edema. Regardless of the etiology and in addition to the macular thickening, the resulting visual acuity depends on many factors, such as duration of edema, perfusion of macular capillaries, photoreceptor loss, retinal pigment epithelium dysfunction, and media opacities.

Histology

Most commonly, macular edema results from pathologic hyperpermeability of retinal blood vessels, particularly the retinal capillary bed. Increased vascular permeability provokes extravasation of fluid, proteins, and other macromolecules in the retinal interstitium. The central area of the retina is predisposed to develop an edema due to its unique anatomy characterized by its increased metabolic activity, loose bindings of the inner connecting fibers in the outer plexiform layer, and the watershed arrangement between the choroidal and retinal circulation with Henle's fiber layer functions as the lateral border. The accumulation of fluid mainly occurs in the outer plexiform layer and the inner nuclear layer. Intracellular accumulation is also found in the Müller cells.

Immunohistochemistry

Numerous molecules may induce the retinal vascular hyperpermeability that leads to macular edema. Depending on the underlying disease entity, these include prostaglandins and leukotrienes, protein kinase C, nitric oxide, and various

cytokines such as vascular endothelial growth factor, tumor necrosis factor alpha, insulin-like growth factor 1, and interleukins.

Optical Coherence Tomography

In the diagnosis and assessment of macular edema, optical coherence tomography (OCT) allows the detection of subretinal and intraretinal fluid and abnormal exudation from the retinal capillary bed. It permits the measurement of foveal retinal thickness and changes in macular edema.

Molecular Diagnostics

Molecular diagnostics exists for a rare cause of macular edema: autosomal dominant cystoid macular edema.

Differential Diagnosis

Inflammatory disorders: intraocular surgery, Irvine-Gass syndrome (cataract surgery), laser procedures, uveitis syndromes, neuroretinitis, idiopathic retinal vasculitis
Retinal vascular disease: diabetic retinopathy, radiation retinopathy, retinal venous occlusion, hypertensive retinopathy, retinal macroaneurysm, macular telangiectasis, Coats' disease
Choroidal vascular disease: choroidal vascular disease, age-related macular degeneration, myopic macular degeneration, etc.
Drug reaction: prostaglandin analogs, epinephrine, nicotinic acid, tamoxifen, thiazides
Retinal dystrophies: retinitis pigmentosa, autosomal dominant cystoid macular edema
Tractional maculopathies: vitreomacular traction syndrome
Retinal detachment: rhegmatogenous, exudative
Intraocular tumors: hemangioma, choroidal malignant tumors, metastasis
Optic nerve abnormalities: cavitary disk anomalies
Idiopathic macular edema

Cross-References

- ▶ Central Retinal Vein, Occlusion of
- ▶ Choroidal Neovascularization
- ▶ Corneoretinal Dystrophy, Bietti's Crystalline
- ▶ Diabetic Retinopathy
- ▶ MS-Associated Uveitis
- ▶ Optic Nerve Edema

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Macular Holes

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Definition

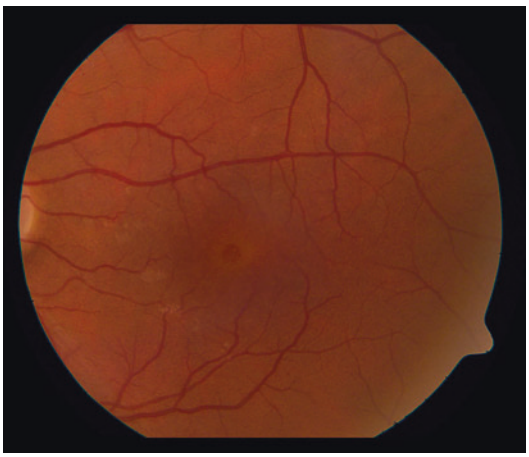
A full thickness defect of the neurosensory retina in the macula region.

Etiology

Most macular holes are idiopathic (Gass 1997; Ho 1999). These holes likely develop from tangential vitreous traction on the fovea. Four stages

of macular hole evolution have been described by Gass (1997). Stage 1 represents an impending macular hole and is further subdivided into stage 1A (detachment of the foveola) and 1B (detachment of the fovea). Approximately, 60% of Stage 1 holes undergo spontaneous resolution and do not progress to Stage 2. Stage 2 follows Stage 1 and is defined as a small full thickness defect in the retina less than 400 micrometers (um) in diameter. The majority of Stage 2 holes progress to Stage 3 holes which are larger (equal to or greater than 400 um) and display a rim of thickened and slightly elevated retina. Stage 4 is defined as a full thickness macular hole in the presence of a posterior vitreous detachment as signified by a Weiss ring (Figs. 1 and 2).

A minority of macular holes develop as sequelae of various vitreoretinal disorders, including trauma, post laser light exposure, lightning strike, hypertensive retinopathy, and cystoid macular edema. The pathogenesis of these secondary macular holes varies according to underlying retinal disease. Macular holes following cystoid macular edema likely develop as the cystic retinal space coalesce and rupture into the vitreous cavity. The cystic retinal edema can be from any etiology, including postsurgical inflammation, infection, uveitis, retinal vascular disease, epiretinal membrane, or chronic retinal detachment. Macular hole following laser light exposure likely develops due to tissue atrophy.



Macular Holes, Fig. 1 Color fundus photograph demonstrating a Stage 3 idiopathic macular hole

Clinical Presentation

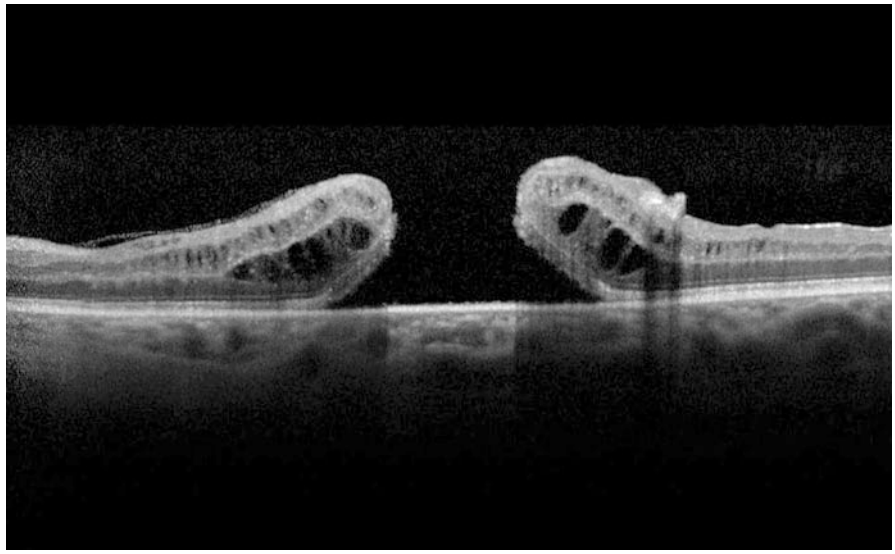
Presenting signs for a macular hole vary according to etiology and stage. Symptoms with idiopathic Stage 1 holes are usually limited to metamorphopsia and a mild decrease in central visual acuity (20/25–20/60). Symptoms from Stage 2 holes are variable and in some cases may actually be less bothersome than those with a Stage 1 hole. Stage 3 holes usually produce significant vision loss with formation of a central scotoma. Stage 4 holes may be associated with new complaint of a "floater" due to the Weiss ring, although patients with poor vision may not notice this.

Diagnostics

Diagnosis of macular hole is made with slit lamp biomicroscopy and confirmed with optical coherence tomography. Stage 1 holes demonstrate loss of the foveal depression with a central yellow spot (Stage 1A) or yellow ring (Stage 1B). Stage 2 and 3 macular holes demonstrate a full thickness retinal defect, while Stage 4 holes involve a Weiss ring in the midvitreous. The clinical Watzke-Allen test is said to be positive if the patient describes a break in a thin beam of light placed on the fovea during slit lamp biomicroscopy. In cases of nonidiopathic macular holes, fluorescein angiography and optical coherence tomography are helpful for identifying any underlying or associated causes, such as cystoid macular edema or epiretinal membrane.

Differential Diagnosis

Differential diagnosis of a macular hole includes cystoid macular edema, solitary drusen, epiretinal membrane with pseudohole, central serous retinopathy, age-related macular degeneration, and solar retinopathy.



Macular Holes, Fig. 2 Optical coherence tomography demonstrating a full thickness Stage 3 macular hole

Prophylaxis

Although no effective prophylaxis against idiopathic macular hole formation is known, prior vitrectomy with removal of cortical vitreous may help decrease risk of hole formation by decreasing the risk of tangential vitreoretinal traction.

Therapy

Pars plana vitrectomy with removal of posterior cortical vitreous and intraocular gas tamponade remains standard of care for symptomatic full thickness macular holes. Peeling of the internal limiting membrane of the retina during vitrectomy is likely beneficial but remains controversial. Success rate of hole closure following vitrectomy surgery ranges from 92% to 100% (Gass 1997; Ho 1999; Sjaarda and Thompson 2006; Wendel et al. 1999).

Prognosis

The prognosis for a macular hole varies according to preoperative visual acuity, stage of hole formation, and underlying etiology. Stage 1 holes undergo spontaneous resolution in up to 60% of cases. Stage 2 through 4 holes can enjoy an improvement in visual acuity following surgical closure in up to 80% of eyes. It has been observed that eyes with a preoperative visual acuity worse than 20/60 improve the most, while eyes with a preoperative acuity better than 20/60 obtain the best final vision. Traumatic macular holes tend to have a worse prognosis than idiopathic macular holes, likely due to associated ocular injury. For almost all eyes following hole closure, vision rarely returns to normal, and some metamorphopsia persists despite visual gains.

Epidemiology

The exact epidemiology of macular holes is unknown. However, idiopathic macular holes occur primarily in the sixth through the eighth decades of life and are more common in women than men.

Cross-References

► Angiography, Fluorescein
► Atrophic Retinal Holes

- ▶ Drusen
- ▶ Pars Plana Vitrectomy
- ▶ Vitrectomy

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Macular Pucker

▶ Cellophane Maculopathy

Macular Swelling

▶ Macular Edema

Macular Thickening

▶ Macular Edema

Macular Xanthophyll

▶ Lutein

Madras Eye

▶ Conjunctivitis

Magendie-Hertwig Sign

▶ Alternating Skew Deviation

Malar Bone

▶ Zygomatic Bone

Malar Complex Fracture

▶ Zygomatic-Maxillary Complex Fractures

Malattia Leventinese (ML)

▶ Doyne's Honeycomb Dystrophy

M

Malignant Glaucoma

▶ Ciliary Block (Malignant) Glaucoma, Muscarinic Antagonists for

Malignant Melanoma (MM)

▶ Melanoma of the Eyelid

Malignant Mesenchymal Tumor of Orbit

▶ Sarcoma, Orbital

Malingering

▶ Nonorganic Visual Loss

Mandibular Division of the Trigeminal Nerve

▶ V3 (Mandibular Nerve)

Mandibular Nerve

▶ V3 (Mandibular Nerve)

Mandibulofacial Dysostosis

▶ Treacher Collins-Franceschetti Syndrome (Mandibulofacial Dysostosis)

Manual Phacofragmentation

▶ Phacofragmentation

Map-Dot-Fingerprint Dystrophy

▶ Corneal Dystrophies

Map-Dot-Fingerprint Dystrophy (Epithelial/Anterior Membrane Dystrophy)

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Synonyms

Anterior basement membrane dystrophy; Cogan microcystic epithelial dystrophy; Epithelial basement membrane dystrophy

Definition

Map-dot-fingerprint dystrophy falls into the category of epithelial dystrophies. As a dystrophy, it is a bilateral disease and can be inherited. This condition is defined by a thickened basement membrane that extends into the epithelium and forms "maps" and "fingerprint" lines. Abnormal epithelial cells can degenerate, forming cystoid spaces, or "dots."

Etiology

The inheritance pattern of this dystrophy appears to be autosomal dominant with incomplete penetrance, but most cases are sporadic (American Academy of Ophthalmology 2012a). A subset of patients has a mutation in the *TGFBI* gene (also referred to as *Big-H3*). The involved gene, on locus 5q31, encodes for a protein responsible for cell adhesion. The functional loss of this protein results in poor attachment of the epithelium to the epithelial basement membrane.

Clinical Presentation

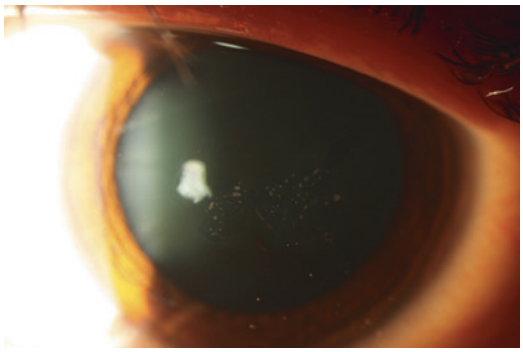
Patients with map-dot-fingerprint dystrophy are generally asymptomatic but can present with symptoms of recurrent corneal erosion, including pain and blurred vision. Other symptoms include tearing, foreign body sensation, and photophobia. These patients will complain of pain on awakening or pain that awakens the patient from sleep. The duration and severity of the pain can vary. Eye rubbing can initiate erosions and exacerbate symptoms. The unpredictable nature of recurrent corneal erosions can be emotionally stressful for patients.

Diagnosis

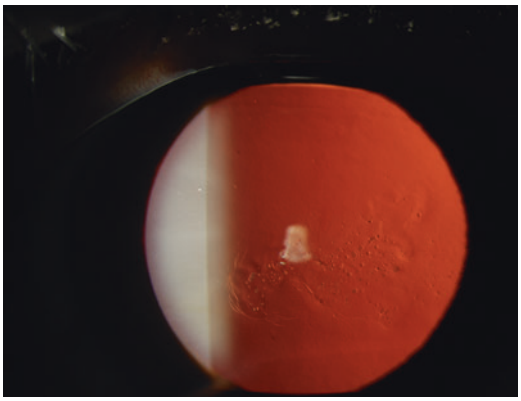
The diagnosis of map-dot-fingerprint dystrophy can generally be made on the slit-lamp examination. Clinical findings including microcysts, gray patches, and linear lesions can be appreciated

by various examination techniques, such as retroillumination, sclerotic scatter, and broad beam illumination. A bilateral exam looking for these clinical features should always be performed, as unilateral findings are more likely related to trauma-associated recurrent corneal erosion syndrome. Both fingerprint lines and map lines are identified in patients with map-dot-fingerprint dystrophy and are differentiated based on morphology. Fingerprint lines are fine lines arranged in a somewhat concentric pattern, whereas map lines are thicker and resemble geographic structures that can be found on maps (Fig. 1). These lines are associated with microcysts in the clinical appearance of patients with this dystrophy (Fig. 2).

Histopathologic findings can aid in diagnosis of map-dot-fingerprint dystrophy, particularly in cases where clinical findings can mimic intraepithelial dysplasia. A thickened epithelial basement membrane is one histopathologic feature that is typical of this epithelial dystrophy (American Academy of Ophthalmology 2012b). Other features include abnormal epithelial cells with absent or abnormal hemidesmosomes and fibrillar material between the basement membrane and Bowman layer.



Map-Dot-Fingerprint Dystrophy (Epithelial/Anterior Membrane Dystrophy), Fig. 1 Map-dot-fingerprint dystrophy, displaying fingerprint lines and microcysts



Map-Dot-Fingerprint Dystrophy (Epithelial/Anterior Membrane Dystrophy), Fig. 2 Map-dot-fingerprint dystrophy, retroillumination view highlights fingerprint lines and microcysts

Differential Diagnosis

The differential diagnosis for map-dot-fingerprint dystrophy is limited. The condition that most commonly mimics map-dot-fingerprint dystrophy is recurrent corneal erosion syndrome from trauma. Studies have found that whereas only 10% of patients with map-dot-fingerprint dystrophy develop recurrent corneal erosions, almost 50% of patients with recurrent corneal erosions have a diagnosis of this epithelial dystrophy. The best way to distinguish traumatic causes of recurrent corneal erosion from those associated with map-dot-fingerprint dystrophy is to do a thorough bilateral exam looking for clinical exam findings such as fingerprint and map lines and microcysts. Traumatic recurrent corneal erosions will most often have findings limited to one eye, whereas map-dot-fingerprint dystrophy will be bilateral.

The nature of traumatic injury that predisposes an eye to recurrent corneal erosion is usually a sharp, sudden injury such as a fingernail poke to the eye. The superficial abrasion heals rapidly but incompletely, making the eye vulnerable to periodic subsequent erosions with minimal to no inciting trauma. Clinical findings during the acute event can include corneal edema and heaped-up epithelium. Oftentimes, however, the epithelial surface has already completely healed at the time of the examination.

Prophylaxis

In order to prevent the occurrence of recurrent corneal erosions in patients with map-dot-fingerprint dystrophy, treatment with 5% sodium chloride drops or ointment can be used at nighttime. In a similar way, lubricating drops or ointment at nighttime can be used. The mechanism of prophylaxis is to create a barrier between the fragile epithelium and the palpebral conjunctiva such that the risk of disrupting the loosely attached epithelium on eyelid opening is minimized.

Therapy

Management of patients with map-dot-fingerprint dystrophy can be classified as medical treatment of acute attacks of recurrent corneal erosion and surgical ablation. The traditional approach to treatment is frequent lubrication, antibiotic ointment, and cycloplegia. In some cases, a bandage contact lens can be beneficial to facilitate healing and to limit pain. Epithelial debridement at the time of acute corneal epithelial erosions can help replace unhealthy epithelium and prevent future episodes. Oral analgesics may also be necessary for the first 24 h after the start of corneal epithelial erosions.

Surgical management should be considered for recalcitrant cases. One effective option is anterior stromal micropuncture. In this procedure, the cornea is punctured about 0.1 mm using a bent 20- or 25- gauge needle in order to create subepithelial scarring and better adhesion of the epithelium to more posterior layers. The central visual axis should be avoided in this procedure in order to limit scarring that can reduce visual acuity. Phototherapeutic keratectomy (PTK) using an excimer laser is another popular option for surgical management of patients with map-dot-fingerprint dystrophy. In this procedure, a large, shallow area of epithelial and anterior Bowman layer ablation is performed. PTK can be used for central erosions but may need to be repeated in 13–44% of cases secondary to a return of symptoms. Other less commonly used surgical approaches to the management of this condition are the Nd/Yag laser and the diamond burr (Aldave 2009). Again, care should be taken to avoid the central visual axis.

Prognosis

The prognosis of patients with map-dot-fingerprint dystrophy is good. Most patients are able to maintain good visual function, except during acute attacks of recurrent corneal erosion.

Epidemiology

Map-dot-fingerprint dystrophy occurs in 6–18% of the population, making it one of the most commonly encountered corneal dystrophies. It occurs more frequently in women and in patients over the age of 50 years.

Cross-References

▶ Corneal Dystrophies
▶ Superficial keratectomy

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MAR

▶ Minimum Angle of Resolution/Recognition (MAR)

Marcus Gunn Pupil

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Synonyms

Relative afferent pupillary defect (RAPD)

Definition

Marcus Gunn pupil or relative afferent pupillary defect (RAPD) presents as a disturbance to the consensual light reflex. In healthy eyes, the reaction of the pupils in both eyes is connected. In other words, a bright light shone into one eye leads to an equal constriction of both pupils (direct and consensual response). When the light source is taken away, the pupils of both eyes enlarge equally (Broadway 2012). In a patient with a RAPD, the pupil of the eye with afferent lesion (e.g., the retina or optic nerve disorder) will constrict less than the other pupil and its corresponding direct response will be less than the consensual response from the fellow eye. Thus, when the light swings (i.e., swinging flashlight test) from the affected pupil to the normal pupil, the pupils both constrict and when the light swings back to the affected pupil the pupils both dilate (i.e., an RAPD).

Etiology

The Marcus Gunn pupil can occur in any lesion affecting significant retina, optic nerve, or optic tract involving the afferent pupillary pathway.

Occurrence

Marcus Gunn pupil can occur in any age, either gender, and any racial group depending on the underlying etiology.

Classification

Marcus Gunn pupil is classified as a pupillary disorder.

Cross-References

- ▶ Afferent Pupillary Defects, Relative (Marcus Gunn Pupil)
- ▶ Anisocoria: Big Pupil
- ▶ Anisocoria of the Small Pupil
- ▶ RAPD (Relative Afferent Pupillary Defect)
- ▶ Relative Afferent Pupillary Defect (RAPD)

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Marfan Syndrome

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Definition

Marfan syndrome (MFS) is a multisystem disorder with manifestations typically involving the cardiovascular, skeletal, and ocular systems (De Paepe et al. 1996; Dean 2007). It was first described more than 100 years ago by a French pediatrician, Antoine-Bernard Marfan, who reported the association of long slender digits and other skeletal abnormalities in a 5-year-old girl, Gabrielle. It is the second most common inherited connective tissue disorder, after osteogenesis imperfecta. It is characterized by musculoskeletal abnormalities, cardiovascular disease, and ocular abnormalities, and it can affect many structures of the eye.

Etiology

Transmission of MFS is autosomal dominant with high penetrance, although approximately 25–30% of cases are sporadic (Frydman 2008). Although abnormalities with fibrillin 1 (FBN1) are responsible for the Marfan phenotype in approximately 80% of patients, MFS can also be caused by inactivation mutations in TGF-β receptor 2 (TGFBR2). FBN1 is a main component of extracellular microfibrils found in a wide range of tissues. FBN1 is coded for on chromosome 15 in the q21.1 locus, and TGFBR2 is located at 3p24.2-p25. Currently, more than 500 mutations of FBN1 have been identified and almost all are unique to an affected individual or family. However, even with the same mutation there is clinical heterogeneity among individuals. Not all patients with MFS are tall and thin with long fingers and pectus excavatum. Patients may appear phenotypically normal with only ocular signs, such as dislocated lenses, to suggest the diagnosis.

Clinical Presentation

MFS remains a clinical diagnosis and is established when sufficient features are present.

The main ocular features of MFS, all of which can result in decreased vision, include bilateral ectopia lentis, myopia, and retinal detachments (Nahum and Spierer 2008). About 50% of patients with MFS are diagnosed by an ophthalmologist; some individuals may present with ocular signs suggestive of this syndrome. The presence of ectopia lentis is considered a major criterion for the diagnosis of MFS.

The most striking physical features of patients with MFS are the musculoskeletal defects. The extremities are disproportionately long for the size of the trunk, and patients are usually tall. Overgrowth of the ribs can deform the chest wall causing pectus excavatum or pectus carinatum. Fingers are disproportionately long and thin (arachnodactyly). Kyphoscoliosis is common and can be progressive. Acetabular protrusion and joint laxity are other skeletal manifestations. A generalized muscular hypotony and joint contracture may occur.

Cardiovascular manifestations of MFS include dilations of the aorta at the level of the sinuses of Valsalva, and the predisposition for aortic tear and rupture. These severe complications are the major cause of morbidity and mortality and are the central target for therapy. Mitral valve prolapse, tricuspid valve prolapse, and enlargement of the proximal pulmonary artery are other common but minor criteria for diagnosis.

Integumental manifestations are mainly skin stretch marks (striae) in the absence of rapid weight gain, and recurrent herniae are common minor manifestations.

Progressive lumbosacral dural ectasia is a major diagnostic criterion. This age-dependant feature is present in 92% of patients. Dural ectasia is usually asymptomatic but can lead to bone erosion and nerve entrapment, resulting in low back pain and proximal leg pain, weakness, und numbness. Dural ectasia is the second most common major criterion and can contribute to an unequivocal diagnosis in 23% of cases.

Pulmonary manifestations include spontaneous pneumothorax and apical blebs.

Diagnostics

The last version of diagnostic criteria for MFS is the Ghent criteria published in 1996. This nosology unequivocally diagnoses or excludes Marfan in 86% of cases. The Ghent criteria are divided in seven areas: cardiovascular system, skeletal system, dura mater, pulmonary system, skin and integument, and family or genetic history. For diagnosis, a major criterion in two different areas as well as involvement of a third area are required for an index case. For a family member, presence of a major criterion in the family history and one major criterion in an organ system and involvement of a second organ system is required. The major ocular criterion is ectopia lentis, and the minor ocular criteria include abnormally flat cornea, increased axial length of globe, and hypoplastic iris or ciliary muscle causing decreased miosis. Of the many ocular abnormalities seen in MFS, by far the most common is ectopia lentis, occurring in 50–80% of affected individuals. Ectopia is usually bilateral, symmetric, and nonprogressive. Abnormal production, distribution, and attachment functions of fibrin-rich zonules, as well as their increased susceptibility to proteolytic cleavage have been proposed to play a role in the pathogenesis of ectopia lentis in MFS (Nemet et al. 2006). The dislocation may be subtle and detectable only by observation of phakodonesis or iridodonesis, sometimes visible by gonioscopy. A forward dislocation of the lens into the pupil or anterior chamber may cause pupillary block with acute glaucoma or chronic angle-closure glaucoma. Posterior dislocation can cause harmful vitreous traction on the retina. Premature cataracts and other lens or capsule opacities can also be found in MFS patients. The second most common ocular manifestation in MFS is myopia, which is found in 34–44% of MFS. Retinal detachment continues to be the most serious ocular complication of MFS, occurring in 5–11% of patients. However, the incidence of retinal detachment increases to 8–38% in the presence of ectopia lentis. There is also a high incidence of bilateral retinal detachments, occurring in up to 69% of patients with retinal detachments. Strabismus is a frequent (19–45%) finding in individuals with MFS (compared to 3–5% in the general population). Delayed and inadequate correction of refractive errors that compromise visual input and deficient fibrillin in extraocular muscle pulleys that cause their instability may be the cause of this high incidence. Glaucoma (most common primary open-angle glaucoma) will develop in about 35% of MFS patients during their lifetime. Patients with MFS may have thinner and flatter than average corneas, and megalocornea may also be present. Hypoplastic iris or ciliary muscle causing decreased miosis can be seen and are considered minor criteria.

Differential Diagnosis

Loeys-Dietz syndrome, mutations in TGFRB1 cause aortic aneurisms and a marfanoid phenotype. While aortic dilation is common to both MFS and Loeys-Dietz syndrome, in the latter, ectopia lentis is rare and the patients display ocular hypertelorism (90%), cleft palate or uvula (90%), and arterial tortuosity (84%). Differential diagnosis of the ocular symptoms are Stickler syndrome, homocystinuria, Ehlers-Danlos syndrome, Weill-Marchesani syndrome, autosomal dominant ectopia lentis, and autosomal recessive ectopia lentis with or without ectopic pupils.

Prophylaxis

Beta-adrenergic receptor blockade to delay or prevent aortic aneurysm and dissection is currently regarded as the standard of care of practice for Marfan patients. Aortic growth is slowed in response to treatment but cannot be stopped. Thus, yearly measures of aortic dimensions should be monitored, and if significant dilatation is present, monitoring should be more frequent. Patients with MFS should undergo comprehensive yearly assessment by an ophthalmologist experienced in this disorder. Patients with MFS should be counseled not to engage in contact sports, competitive athletics, or isometric exercise because of increased risk of aortic dilation and

rupture. Pregnancy imposes a risk of aortic enlargement and rupture. The risk is related to the size of the aortic root before risk. If the aortic root measures less than 4 cm, the pregnancy is low.

Therapy

When the aortic diameter reaches 5 cm elective cardiovascular surgery is recommended. In recent years, surgical attempts to maintain the native aortic valve showed encouraging results and is now the preferred surgical treatment, particularly for women in the childbearing age.

Indication for surgical lens extraction include lens opacity with poor visual function, anisometropia or refractive error not amenable to optical correction (i.e., when the equator of the lens is exactly in the optic axis), impending complete luxation and lens-induced glaucoma or uveitis. Lensectomy with limited anterior vitrectomy and subsequent correction of aphakia with glasses or contact lenses has been used for children with ectopic lenses with excellent results. Because of zonular weakness and the resultant capsular instability, correction of aphakia with implantation of an intraocular lens in ectopia lentis is challenging. Options include anterior chamber IOL (iris or chamber angle support), ciliary sulcus posterior chamber IOL fixed to the sclera and/or to the iris, and scleral fixated capsular tension rings. In children, angle-supported anterior chamber lenses and also ciliary sulcus posterior chamber lenses have a high incidence of complications and should therefore be avoided.

Prognosis

In the 1970s, life expectancy of patients with MFS was reduced secondary to the increased risk for dissection and rupture of the ascending aorta. Over the past 30 years, improvement of diagnostic modalities and aggressive medical and surgical therapy for general and ophthalmlic pathology have resulted in considerable improvement of life expectancy and quality of patients with MFS.

Epidemiology

The estimated incidence is between 1/5000 and 1/20,000, and about 25–30% of cases represent new mutations.

Cross-References

▶ Ectopia Lentis

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Marginal Keratitis

▶ Catarrhal (Marginal Corneal) Infiltrates

Maroteaux-Lamy Syndrome

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Synonyms

Arylsulfatase B deficiency, ASB deficiency; MIM # 253200; Mucopolysaccharidosis type VI; MPS VI, MPS 6; *N*-Acetylgalactosamine-4-sulfatase deficiency

Definition

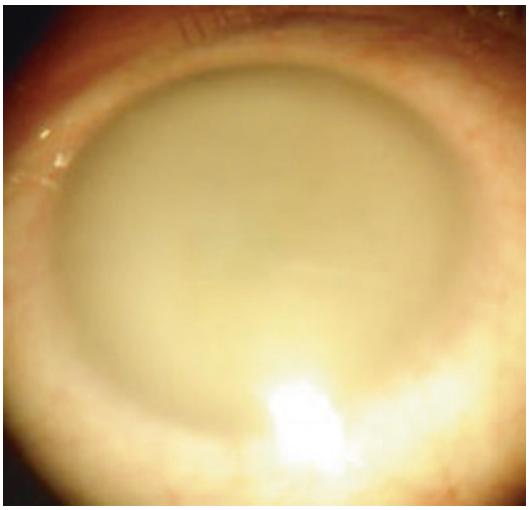
Maroteaux-Lamy syndrome (MPS VI) is an autosomal recessive lysosomal storage disease. Mutations in the arylsulfatase B gene on chromosome 5 cause decreased or absent activity of the enzyme arylsulfatase B (ASB), also called *N*-acetylgalactosamine-4-sulfatase, leading to incomplete degradation and accumulation of the glycosaminoglycan (GAG) dermatan sulfate and cell injury.

Etiology

MPS VI is an autosomal recessive disease from mutations in chromosome 5, position 5q13–5q14. Clinical disease is a result of progressive accumulation of dermatan sulfate in lysosomes, cells, and tissues and manifests only when enzymatic activity is less than 10% of the lower limit of normal.

Clinical Presentation

Phenotypic presentation is varied but typically presents as a rapidly or slowly progressing form, with severity of clinical presentation dependent upon the amount of functional enzymatic activity. The rapidly progressing form usually presents before 3 years of age, while disease may not present until the second or third decade in milder forms. Ophthalmologic findings are present in nearly all patients with Maroteaux-Lamy syndrome at some point in the disease. Progressive corneal clouding occurs in 95% of patients with MPS VI due to accumulation of dermatan sulfate in corneal epithelium, stroma, and endothelium (Ashworth et al. 2006). Clouding is typically more severe than in MPS I and is described as having a ground-glass appearance (Fig. 1). Corneal haze results from GAG accumulation, anterior stromal scarring, abnormal keratocyte morphology, and alteration of collagen fibril arrangement (Alroy et al. 1999). Narrowing of the anterior chamber and poor pupillary dilation may occur secondary to deposition of dermatan sulfate in the trabecular meshwork and iris stroma. Abnormalities in the optic disk are reported to occur in 50% and may be secondary to increased intraocular pressure, GAG accumulation in ganglion cells, or increased intracranial pressure (ICP) causing disk edema (Ashworth et al. 2006). Optic atrophy is reported in 15% and may be related to compression of the optic nerve by thickened dura or bony narrowing along the optic canal.

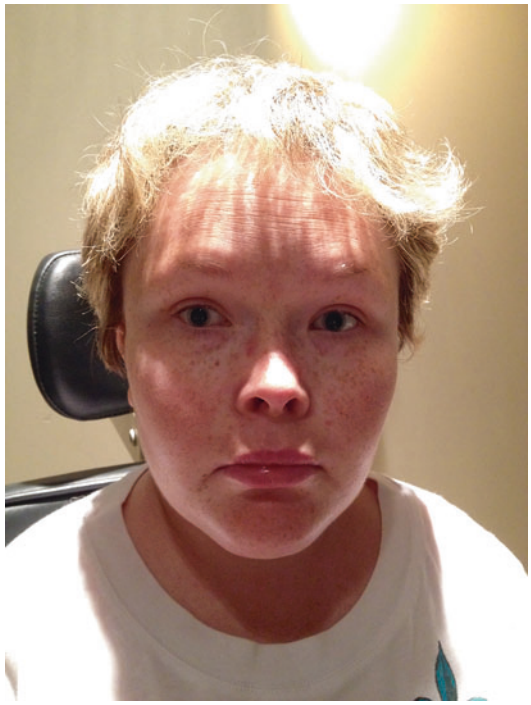


Maroteaux-Lamy Syndrome, Fig. 1 Corneal clouding in patient with Maroteaux-Lamy syndrome

Systemic manifestations are numerous and include short stature, skeletal deformities (dysostosis multiplex, kyphosis or scoliosis, and degenerative joint disease), coarse facial features (large head, frontal bossing, depressed nasal bridge, enlarged tongue, gingival hyperplasia), hepatosplenomegaly, inguinal and abdominal hernias, middle ear disease and deafness, cardiac valve disease, reduced pulmonary function, sleep apnea, carpal tunnel disease, cervical spine instability, meningeal thickening, and communicating hydrocephalus, among others (Fig. 2). Patients with MPS VI are of normal intellect, which helps distinguish this syndrome from other forms of MPS (Valayannopoulos et al. 2010).

Diagnosis

Diagnosis is usually suspected from the conglomeration of clinical findings but may be difficult to

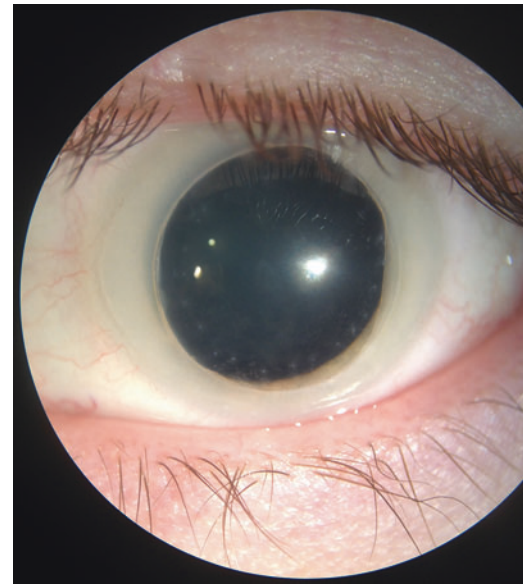


Maroteaux-Lamy Syndrome, Fig. 2 Facial features in patient with MPS VI

detect because of variable presentation, especially in milder forms of disease. Confirmation of fibroblast or leukocyte ASB enzyme activity less than 10% of the lower limit of normal is required for diagnosis (Valayannopoulos et al. 2010). Demonstration of normal activity of a different sulfatase enzyme is also required as it excludes a diagnosis of multiple sulfatase deficiency. Supporting findings for MPS VI include elevated urinary dermatan sulfate, evidence of dysostosis multiplex radiographically, and demonstration of intermediate levels of leukocyte ASB enzyme activity in both parents to support their diagnosis as carriers. Prenatal testing is possible but is limited to those who already have a child with MPS VI.

Differential Diagnosis

- MPS I (Hurler, Scheie, Hurler-Scheie), II (Hunter), IVA (Morquio), and VII (Sly)
- Mucolipidosis I (sialidosis), II, III, and IV
- Multiple sulfatase deficiency (MSD)



Maroteaux-Lamy Syndrome, Fig. 3 Clear graft post-penetrating keratoplasty. Note host corneal clouding

Prophylaxis

Enzyme replacement therapy (ERT) and hematopoietic stem cell transplant can delay progression of clinical symptoms, and avoidance of consanguinity is beneficial.

Therapy

Systemically, ERT with intravenous galsulfase (Naglazyme) effectively replaces the ASB enzyme, but it is unable to reach the central nervous system and cornea due to the blood-brain barrier. Hematopoietic stem cell transplant is also used to replenish the deficient enzyme. Ophthalmologic therapy is directed at control of corneal clouding and glaucoma. Penetrating keratoplasty can be successful, although dermatan sulfate does reaccumulate in the graft at variable rates with resultant corneal clouding (Fig. 3; Bothun et al. 2011). Topical glaucoma medications treat increased intraocular pressure.

Prognosis

Prognosis is variable and depends upon age of onset, rate of disease progression, and age at initiation of ERT. A urine GAG above 100 ug/mg creatinine is a poor prognostic sign (Valayannopoulos et al. 2010). Patients with the slowly progressing form may survive until the third decade or later.

Epidemiology

MPS VI is estimated to occur in 1 in 240,000–400,000 persons worldwide (Valayannopoulos and Wijburg 2011). MPS VI accounts for 2–4% of all MPS in Scandinavia, 3% in the Netherlands, 16% in Portugal, and 18.5% in Brazil. A common mutation 1533del23 in certain populations confers increased risk, as does consanguinity (Valayannopoulos et al. 2010).

Cross-References

- ▶ Hurler-Scheie Syndrome
- ▶ Morquio Syndrome
- ▶ Mucopolysaccharidosis

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Maxillary Complex Fracture

- ▶ Zygomatic-Maxillary Complex Fractures

Maxillary Division of the Trigeminal Nerve

- ▶ V2 (Maxillary Nerve)

Maxillary Fracture

- ▶ Guerin (Maxillary) Fracture

Maxillary Fractures

- ▶ Le Fort Fractures

Maxillary Nerve

- ▶ V2 (Maxillary Nerve)

Maxillary Roof Fracture

- ▶ Blowout Fractures

Maximum Depth Deep Anterior Lamellar Keratoplasty

- ▶ Deep Anterior Lamellar Keratoplasty (DALK)

McCannel Technique

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Synonyms

Iris suture fixation

Definition

A technique developed in 1976 by Malcolm McCannel, MD, for iris suture fixation for posterior chamber intraocular lenses

Indication

The technique was developed for refixing, resuturing, and stabilizing subluxated posterior chamber intraocular lenses and maintaining iris integrity (Karmel 2014). The procedure is considered if there is insufficient capsular or zonular support or excessive iris defect. This procedure served as a transcorneal, retrievable suture technique.

Contraindication

Though safe, contraindications to cataract surgery are an indication for not pursuing the McCannel technique. The absence of sufficient iris tissue is a contraindication.

Techniques and Principles

The technique is a form of iris suturing that entails passing a long needle on a 10-0 polypropylene suture into the proximal and distal ends of the iris (Krachmer et al. 2011). Following this, the needle tip is guided out of a distal paracentesis by docking into a cannula. After this step, both suture ends are then passed through another paracentesis adjacent to the desired knot position. The knot is then secured and cut close to the surface of the tissue. The knot and iris may then be repositioned if needed. These steps are repeated to secure a defect. Modifications to this suturing technique have been developed to enhance the stability of the lens and iris.

Outcome

Refixing, resuturing, and stabilization of a subluxated posterior chamber intraocular lens and iris defect repair.

Complications

Epithelialization of the anterior chamber (Abbott and Spencer 1978), perforation, detachment of structures, iris defect, hemorrhage, lens dislocation, corneal irregularities (Yanoff and Duker 2014)

Cross-References

- ▶ Iris defect
- ▶ Phacoemulsification and Posterior Chamber Intraocular Lens (IOL) Implantation

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Medial

- ▶ Canthal Reconstruction

Medial Canthoplasty

- ▶ Y-V-Plasty for Blepharophimosis Syndrome

Medial Epicanthoplasty

- ▶ Y-V-Plasty for Blepharophimosis Syndrome

Medication Misuse Headache

- ▶ Analgesic Rebound Headache

Medication Overuse Headache

▶ Analgesic Rebound Headache

Meesman's Epithelial Dystrophy

▶ Epithelial Dystrophies

Meesmann Dystrophy

▶ Corneal Dystrophies

Meesmann Epithelial Corneal Dystrophy (MECD)

▶ Juvenile Epithelial Dystrophy (Meesmann Dystrophy)

Megalocornea

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Definition

Megalocornea: A term used to describe those eyes that have an enlarged cornea, normal IOP, normal optic disk, and no family history of congenital glaucoma; it often occurs in association with other ocular or systemic abnormalities.

Etiology

Megalocornea is a developmental anomaly of unknown etiology. Several mechanisms of development have been postulated including a defect in the growth of the optic cup which leaves a larger space for the development of the cornea.

Clinical Presentation

1Megalocornea presents as a bilateral enlargement of the cornea, with a horizontal diameter of 12 mm or greater at birth and 13 mm or greater after 2 years of age. There are a few variants of this disorder: autosomal dominant being the least common (and is typically not associated with other ocular abnormalities) and X-linked recessive which is more common (thus, accounting for the increased prevalence in males). The X-linked variant is commonly associated with other ocular findings including iris transillumination defects secondary to pigment dispersion, lens subluxation, arcus, and central crocodile shagreen. Other associations include mental retardation and congenital miosis. The enlargement does not arise from corneal stretching but rather from an overgrowth; and, as such, the endothelial cell count is normal. Corneal clarity and thickness are usually normal as well. This is in stark contrast to the enlarged corneal diameter that can be observed with buphthalmos (which presents as elevated IOP and an enlarged globe). Other findings which differentiate megalocornea from buphthalmos include absence of tears in Descemet's membrane and lack of optic disk cupping.

In addition to associated ocular anomalies, various systemic abnormalities have been observed including multiple malformation syndromes, connective tissues diseases, dermatologic abnormalities, and genetic diseases. As such, it is prudent to perform a thorough pediatric exam and to consult physicians from other disciplines based on the associated findings.

Diagnosis

Various diagnostic modalities can be utilized to differentiate megalocornea from buphthalmos and anterior megalophthalmos:

1. Gonioscopy: lack of a widened ciliary band and lack of excessive mesenchymal tissue in the angle in the presence of an enlarged

anterior segment/cornea helps distinguish megalocornea from the other potential diagnoses such as anterior megalophthalmos.
2. A-scan ultrasound biometry: allows for measurements of the axial length of the eye. Increased axial length can be seen in buphthalmos, whereas a normal to short vitreous length can be seen in megalocornea.
3. Specular microscopy: allows for measurement of the corneal endothelial cell count. Normal counts indicate megalocornea, whereas a decrease in the count is consistent with congenital glaucoma.

Pertinent lab testing entails screening for certain genetic markers. The genetic locus for X-linked megalocornea appears to be in the region Xq21–q22.6.

Differential Diagnosis

- Buphthalmos
- Anterior Megalophthalmos

Prophylaxis

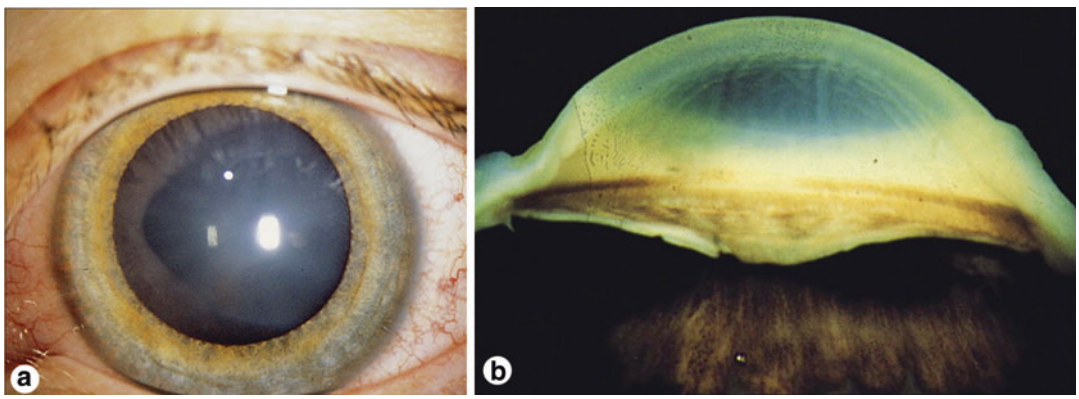
No effective prophylaxis.

Therapy

The condition does not usually require treatment except for management of associated complications including high myopic refractive error, juvenile cataract, and glaucoma. Management of the refractive error is usually via spectacle correction. As for cataracts, this can be challenging given the underlying anterior segment dysgenesis. Various case studies have reported on the success of cataract extraction in patients who have megalocornea; however, care must be taken when considering surgical technique as well as intraocular lens size/type. Another frequently associated complication is secondary glaucoma. Per case reports, elevated IOP usually results from associated spherophakia or ectopic lentis. Thus, surgical treatment for glaucoma secondary to megalocornea is lens removal; this differs from the conventional treatment for primary congenital glaucoma and buphthalmos which requires angle surgery.

Prognosis

Overall prognosis is good; the cornea itself does not continue to enlarge after 2 years of age. There can be associated ocular complications (see sections "Clinical Presentation" and "Therapy")



Megalocornea, Fig. 1 (**a**) Corneal diameters of 14 mm (**b**) Gross specimen showing appearance of enlarged cornea and heavily pigmented trabecular meshwork (Sugar, Joel, Wadia, Hormuz P., Vasaiwala, Roshni A. – Ophthalmology, 173–176.e1 © 2014 Copyright © 2014, Elsevier Inc. All rights reserved)

which are treated accordingly. In the presence of concomitant systemic abnormalities, a more thorough and long-term follow-up needs to be established including scheduled follow-ups with physicians from other specialities.

Epidemiology

Males account for ~90% of cases because of the most common pattern of inheritance (X-linked recessive). According to the literature, 50% of cares are X-linked recessive and 40% are autosomal, whereas the remaining 10% are sporadic. However, the condition itself is rare and the exact incidence is unknown (Fig. 1).

Cross-References

► Keratoglobus Basic Science

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Megalopia

► Macropsia

Meibomian Cyst

► Chalazion

Meibomian Gland Carcinoma

► Sebaceous Carcinoma/Adenocarcinoma

Meibomian Gland Dysfunction

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Synonyms

Meibomianitis; Meibomitis

Definition

It is a common chronic disorder of the meibomian glands and a significant cause of dry eye disease, in which obstruction of the glands and/or abnormalities of glandular secretions occur.

Etiology

Meibomian glands produce the lipid layer of the tear film, which prevents tear evaporation, stabilizes the tear film, and smooths the ocular surface.

Meibomian gland dysfunction (MGD) occurs when the terminal ducts become obstructed. Here, ductal epithelium hyperkeratinization and abnormally viscous meibomian gland secretions, or meibum, block the ducts. This leads to stasis of meibomian gland secretion and inappropriate formation of the lipid layer of the tear film. Consequently, there is an increase in evaporation, instability, and osmolarity of the tear film, with greater bacterial growth on the lid margins, inflammation of the ocular surface, and evaporative dry eye. Factors that affect obstruction of the meibomian glands include age, sex, hormones, and topical medication (Nichols et al. 2011).

Bacterial flora on the eyelids can also contribute to MGD by adversely modifying the lipid composition of the meibum. Bacterial lipases degrade the sterol and wax esters in the meibum, forming inflammatory free fatty acids. This increases the melting point and viscosity of the meibum, causing obstruction of the glands.

Clinical Presentation

Patients with MGD in the early stage may be asymptomatic. As the dysfunction progresses, symptoms of ocular surface irritation and those consistent with dry eyes may manifest, including itching, burning, foreign body sensation, red eyes, photophobia, and filmy vision that is worse in the morning.

Clinical signs of MGD include:

- Meibomian gland orifice plugging and/or posterior displacement
- Meibomian gland dropout or dilation
- Rounded, thickened, erythematous, hyperkeratinized, vascularized, or telangiectatic posterior lid margins
- Excess oil or foam in tear film
- Oily eyelid margins
- Conjunctival injection
- Hordeolum or chalazion
- In severe cases, corneal scarring, thinning, pannus, or neovascularization

MGD can lead to posterior blepharitis and atopic keratoconjunctivitis.

Diagnosis

Routine tests to assess for dry eyes should be conducted, including measuring blink rate, tear volume, tear osmolarity, tear evaporation, tear film breakup time, and tear secretion (Schirmer test). Ocular surface damage can be determined with corneal and conjunctival staining.

Specific tests can be performed to evaluate for MGD. Meibomian gland function is assessed with gland expression using digital pressure over the eyelids. Expressibility and secretion quality of meibum are graded to determine the stage of MGD. Abnormal meibum is excessive, viscous, granular, or toothpaste-like. Meibography, which transilluminates the everted eyelid with infrared photography or video imaging, evaluates for narrowing or occlusion of the orifices, distortion or dilation of the glands, and gland dropout. A meibometer measures meibum excretion. Adhesive tape is used to sample the meibum from the lid margin, and the lipid imprint is analyzed. This is not a commonly performed test in the clinic (Krachmer et al. 2011).

Differential Diagnosis

Keratoconjunctivitis sicca from aqueous-deficient dry eye can present with similar dry eye symptoms as MGD. Tear film examination and Schirmer test can help differentiate the two causes of dry eyes. Although MGD can cause blepharitis, other forms of blepharitis should be ruled out, particularly staphylococcal blepharitis. An internal hordeolum is a staphylococcal infection and inflammation of the meibomian gland that may present similarly but is differentiated by being painful or tender.

Sebaceous carcinoma should be considered in unilateral cases of MGD refractory to therapy with persistent localized inflammation and changes in anatomy, such as loss or distortion of eyelash follicles.

Prophylaxis

Proper daily eyelid hygiene may help reduce the development or recurrence of MGD.

Therapy

Eyelid hygiene is an important long-term treatment of MGD. Warm compresses should be applied to the eyelids for at least 4 min, one to two times a day, in order to break up meibomian gland secretions and crust along the eyelid margin. Lid massage follows the compresses to express secretions. Lid scrub with diluted baby shampoo or eye scrub solution then removes the secretions. Eyelid hygiene maintenance on a long-term basis can effectively treat chronic blepharitis.

Dietary changes are recommended, including increasing intake of omega-3 fatty acids. Environmental changes should be considered, such as improving ambient humidity. If there are symptoms of dry eyes, artificial tears for lubrication may provide relief.

If there are moderate MGD clinical signs and symptoms, consider adding oral tetracyclines for several months, especially if there is concomitant rosacea. Treatment options are oral tetracycline (250 mg four times a day), doxycycline (50–100 mg twice a day), or minocycline (50 mg twice a day). The lipophilic nature of the antibiotic can prevent lipases from altering lipid composition of the meibum.

In more severe cases with significant inflammation of the eyelids, consider using topical antibiotics and anti-inflammatory agents, such as a combination antibiotic-steroid ointment. Topical ciclosporin is used with evidence of posterior blepharitis (Krachmer et al. 2011).

Prognosis

MGD is a chronic disease with frequent recurrences or exacerbations that can negatively affect quality of life with dry eye symptoms. Severe cases can lead to corneal neovascularization. With prompt and appropriate treatment and eyelid hygiene, there can be symptomatic relief and a decrease in recurrences.

Epidemiology

MGD is commonly seen in the clinical setting and is a major cause of dry eye disease. There is variability in the reported prevalence of MGD. The highest prevalence of greater than 60% has been reported in Asian populations, whereas 3.5–19.9% has been reported among Caucasians (Nichols et al. 2011). MGD is more frequent with age and may be a manifestation of meibomian gland degeneration with age.

Risk factors or coexisting conditions that have been associated with MGD include anterior blepharitis, contact lens wear, *Demodex folliculorum*, androgen deficiency, menopause, aging, Sjögren's syndrome, cholesterol levels, psoriasis, atopy, rosacea, hypertension, and benign prostatic hyperplasia (BPH). Medications that can contribute to MGD include antiandrogens, BPH medications, postmenopausal hormone therapy, antihistamines, antidepressants, and retinoids (Nichols et al. 2011).

Cross-References

- ▶ Blepharitis
- ▶ Chalazion
- ▶ Dry Eye
- ▶ Hordeolum
- ▶ Keratoconjunctivitis Sicca
- ▶ Meibomian Glands
- ▶ Pannus/Micropannus
- ▶ Schirmer Tests
- ▶ Sebaceous Carcinoma
- ▶ Tear Film (Tears)

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Meibomian Gland Lipogranuloma

► Chalazion

Meibomian Glands

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Synonyms

Tarsal glands

Definition

Meibomian glands are holocrine-secreting sebaceous glands that are embedded in the tarsal plate of the eyelids. There are approximately 40 glands in the upper eyelid and 25 arranged in a single row behind the eyelashes.

Structure

This type of sebaceous gland is derived from a common pilosebaceous unit that differentiates during the second month of gestation. However, they do not have a hair follicle. A common duct connecting multiple acini runs the length of the gland and emerges anterior to the mucocutaneous junction. The acini are lined by cuboidal epithelium and synthesize lipids, which are excreted onto the ocular surface, as meibum, through the gland orifice. Contraction of the Riolan muscle which surrounds the meibomian gland ducts compresses the duct when the eye is open, thus preventing meibum outflow. Expression of lipid onto the tear film occurs when contraction of the palpebral portion of the orbicularis muscle contracts and milks the glands. Meibum composed of cholesterol, triglycerides, and free fatty acids is principally formed by nonpolar lipid wax and esters and sterol esters. Its unique characteristic provides a low melting point, which allows the meibum to stay liquid at eyelid temperature. Lipid abnormalities can be caused by bacterial lipases produced by *S. epidermidis* and *S. aureus*. The exoenzymes, triglyceride lipase and cholesterol and wax esterase, produced by bacteria alter the composition of meibum and induce pathologic changes representative of meibomian gland dysfunction (MGD) such as dilatation of the ducts, acini enlargement with squamous metaplasia, granuloma formation, increased inflammatory cells, and abnormal keratinization. The meibum in patients with blepharitis contain low levels of unsaturated fatty acid. These fatty acids are very important in maintaining normal meibomian gland secretions.

Function

Meibomian glands are very important in the stability of the tear film. The meibum excreted by the meibomian glands represents the outer lipid layer of the precorneal tear film. Without it excessive tear evaporation leads to disruption of the optically smooth surface necessary for optimal visual acuity.

Clinical Relevance

Meibomian gland dysfunction is a common cause of chronic inflammation of the corneal surface and conjunctiva. The reduced lipid in the tear film and increased eyelid margin

inflammation leads to meibomitis or posterior blepharitis and progressive scarring of the eyelid margin and tarsal conjunctiva. Ocular surface symptoms and signs can include burning, foreign body sensation, tearing, blurred vision, itching, redness, foamy tear film, and irregularity of the lid margin. It can also lead to recurrent chalazia.

Associated ocular surface inflammation is often seen as conjunctival injection, papillary reaction, episcleritis, superficial punctate keratopathy, pannus, corneal epithelial and subepithelial infiltrates, and corneal thinning. Patients with MGD can also have features of rosacea.

Management usually includes warm compresses, eyelid massage, and lid margin cleansing. Oral doxycycline is indicated if symptoms and signs persist. The presence of infiltrates or neovascularization of the cornea may require topical steroids with close monitoring for side effects. Topical antibiotics may be helpful when the bacterial component is significant.

Cross-References

- ▶ Blepharitis
- ▶ Chalazion
- ▶ Dry Eye
- ▶ Meibomian Gland Dysfunction
- ▶ Meibomitis
- ▶ Rosacea: Overview

Further Reading

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Meibomianitis

▶ Meibomian Gland Dysfunction

Meibomitis

▶ Meibomian Gland Dysfunction

Melanin in Eyes

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Definition

High molecular weight pigment present in retinal pigment epithelial cells and choroid. Melanin is produced within melanosomes via the oxidation of tyrosine by tyrosinase. Melanin absorbs radiant energy and improves the retinal image by reducing light scatter and blocking light absorption by the sclera.

Cross-References

- ▶ Age-Related Macular Degeneration
- ▶ Albinism
- ▶ Choroidal and/or Ciliary Body and/or Iris Melanoma
- ▶ Melanosis
- ▶ Retinal Pigment Epithelium

Melanoblastosis Cutis

▶ Bloch-Sulzberger Syndrome (Incontinentia Pigmenti)

Melanocytic Nevus

- ▶ Compound Nevus
- ▶ Nevus, Intradermal
- ▶ Nevus, Junctional

Melanocytosis

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Oculodermal melanocytosis (ODM) was first described by Hulke in 1861 and later by Ota and Fitzpatrick in 1939 and 1956, respectively (Fitzpatrick et al. 1956; Gonder et al. 1982a; Hulke 1860). It is a pigmentary condition of the ocular structures with or without associated pigmentation of the periorbital skin. Rarely the condition can involve pigmentation of the orbit, meninges, CNS, and soft palate (Fitzpatrick et al. 1956; Gonder et al. 1982a; Shields and Shields 2004; Singh et al. 1998). When pigmentation is limited to the ocular structures, the process is termed ocular melanocytosis. With concurrent hyperpigmentation of the periorbital skin, the term oculodermal melanocytosis is used. Recently, the term oculodermal melanocytosis has been utilized to combine the above two descriptions, as both entities involve the common denominator of ocular melanocytosis (Singh et al. 1998).

Signs and Symptoms

Nearly all patients with oculodermal melanocytosis present with pigmentation of the sclera or episclera (Shields et al. 2013; Teekhasaenee et al. 1990a). These changes appear as well-defined, blue fusiform spots deep to the conjunctiva and are visible at random locations on the globe. Hyperpigmentation and heterochromia of the iris in a generalized, and less commonly sectoral, fashion is also seen in a majority (~87.4%) of cases (Teekhasaenee et al. 1990a). Associated hyperpigmentation of the anterior chamber angle is seen in nearly all cases with iris heterochromia. Gonioscopy reveals a heavily pigmented trabecular meshwork with dense, pigmented iris processes. This dense pigmentation of the angle is speculated to be linked with ipsilateral ocular hypertension and glaucoma (Araie et al. 2002; Khawly et al. 1995; Magarasevic and Abazi 2013; Teekhasaenee et al. 1990a). On funduscopic examination, generalized or sectoral choroidal hyperpigmentation, and less commonly hyperpigmentation of the optic disc margin, can be seen. Rarely, patients can present with a fine dusting of pigment on the anterior surface of the lens capsule or the corneal endothelial surface, mimicking a Krukenberg spindle. The classic skin finding, the nevus of Ota, consists of a hyperpigmented, brown to blue patch of skin in the ophthalmic and/or maxillary distributions of the trigeminal nerve.

Epidemiology

Oculodermal melanocytosis is five times more common among females compared to males and is seen more often in Asians than Africans and is least common among Caucasians (Araie et al. 2002; Singh et al. 1998; Teekhasaenee et al. 1990a). However, the incidence of uveal melanoma among Caucasians with ODM is elevated compared to their non-white counterparts (Araie et al. 2002; Teekhasaenee et al. 1990a). Oculodermal melanocytosis has a bimodal distribution with a majority of cases presenting at birth and more rarely during puberty or pregnancy (Gonder et al. 1982b).

Complications

Uveal melanoma is a rare complication of oculodermal melanocytosis. An estimated 1 in 400 patients with ODM has a lifetime risk of developing uveal melanoma (Shields et al. 2013; Singh et al. 1998). This stands in

contrast to the incidence of uveal melanoma in the general population, which is a much lower 1 in 13,000. In addition, ODM patients diagnosed with uveal melanoma have a twofold higher rate of metastatic disease compared to their non-ODM counterparts (Mashayekhi et al. 2013). For this reason it is recommended that patients with ODM are examined twice yearly to screen for signs of uveal melanoma (Shields et al. 2013).

Ocular hypertension is seen in the ipsilateral eye in 10% of oculodermal melanocytosis cases (Araie et al. 2002; Khawly et al. 1995). Melanocytic infiltration of the filtration angle causing reduced aqueous outflow is thought to be the underlying mechanism (Araie et al. 2002; Khawly et al. 1995; Magarasevic and Abazi 2013). However, no linear correlation has been found between the degree of angle pigmentation and the magnitude of elevated intraocular pressure. An equal 10% of ODM cases show an asymmetry of optic nerve cup to disc ratio of 0.2 or greater in the ipsilateral eye (Araie et al. 2002; Khawly et al. 1995; Magarasevic and Abazi 2013).

More uncommonly, oculodermal melanocytosis has been associated with primary orbital melanoma, meningeal melanocytoma, and primary melanoma of the CNS (Doglietto et al. 2012; Hino et al. 2005; Korányi et al. 2000; Löffler and Witschel 1989; Piercecchi-Marti et al. 2002; Radhadevi et al. 2013; Rice and Brown 1990; Rivers et al. 2001).

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Melanokeratosis, Striate

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Definition

Striate melanokeratosis refers to pigment lines located in the epithelium, which extend from the limbus toward the central cornea (Fig. 1).

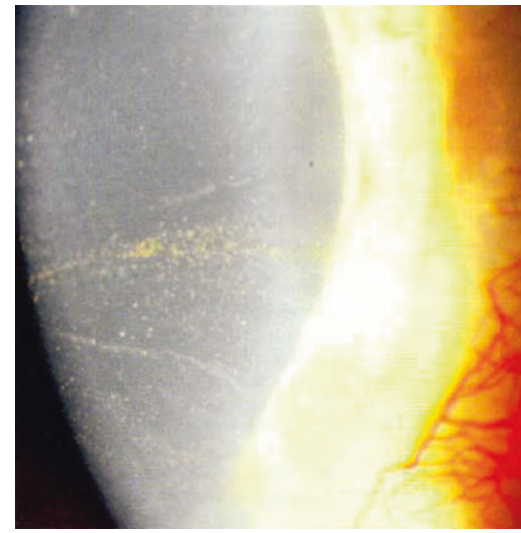
Etiology

Migration of conjunctival melanoblasts into the cornea is the possible etiology. The cornea normally contains no pigmented cells, but melanocytes are present in the limbal area adjacent to blood vessels. It is thought that melanin transfers from these cells to adjacent epithelial cells, which are then carried centripetally forward in the cornea with striate pattern. Injury, cataract extraction, penetrating keratoplasty, inflammation, and subconjunctival usage of 5-fluorouracil are the other possible events predisposing the patients for the migration of melanin or melanoblasts into the cornea and having melanokeratosis (Krachmer et al. 2011).

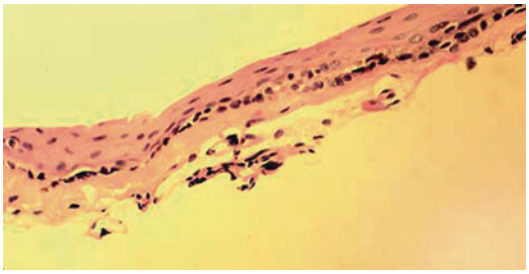
Clinical Presentation

Most commonly it occurs in darkly pigmented individuals but also can occur in lighter pigmented individuals after injury or inflammation. Striate melanokeratosis usually affects black patients with heavy limbal pigmentation and has been described in association with corneal epithelial injury.

Burning sensation can be felt that was due to stimulation of the corneal nerve endings by the



Melanokeratosis, Striate, Fig. 1 Striate Melanokeratosis



Melanokeratosis, Striate, Fig. 2 Corneal biopsy with deposits of melanocytes in the basal layers of the corneal epithelium

invading tissue pigment lines located in the deep layers of the corneal epithelium (Fig. 2). which extend from the limbus toward the center of the cornea, and it tends to assume a curved or whorled form (Lemp 1991; Boto-de-los-bueis et al. 2009).

Diagnosis

Slit lamp exam.

Differential Diagnosis

It could be misdiagnosed with cornea verticillata.

Corneal invasion by pigment can also originate from conjunctival cancerous and precancerous melanosis close to the limbus. Nevus, PAM (primary acquired melanoma), malignant melanoma, and epithelial iron lines are some differential diagnosis of striate corneal melanosis (Boto-de-los-bueis et al. 2009; Krachmer et al. 2011).

Prophylaxis

Unclear.

Therapy

It does not need any treatment except avoiding the stimulus promoted by melanokeratosis.

Prognosis

(Most often) good.

Epidemiology

Unclear.

Cross-References

- ▶ Choroidal and/or Ciliary Body and/or Iris Melanoma
- ▶ Melanosis
- ▶ Primary Acquired Melanosis

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Melanoma of the Eyelid

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Synonyms

Malignant melanoma (MM)

Definition

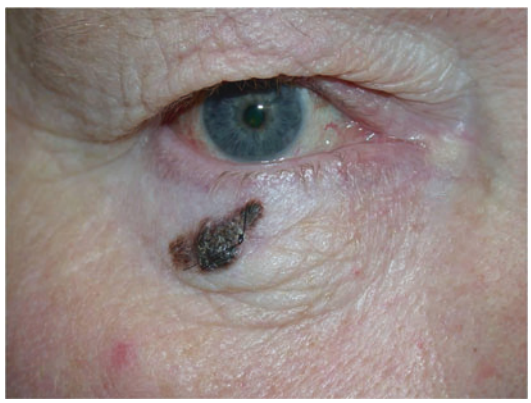
A malignant tumor of melanocytes.

Etiology

Malignant melanoma develops when the melanocytes no longer respond to normal control mechanisms of cellular growth and are capable of invasion locally or spread to other organs in the body (metastasis). Sun exposure definitely increases risk of developing melanoma, especially if a history of severe sunburns during early age is present.

Clinical Presentation

There are several different ▶ types of melanoma, and they vary in appearance. In the eyelid, it can occur in one of the three following forms: superficial spreading malignant melanoma, lentigo maligna melanoma, and nodular melanoma. Lentigo maligna melanoma (LMM) arises in the site of a preexisting lentigo maligna. This lesion is nonpalpable and tan to brown with irregular margins. When dermal invasion occurs, the area becomes elevated and darker (LMN). Nodular melanoma (NM) lesions are slightly elevated, blue-black, or may be amelanotic. MMs tend to be asymmetric, have irregular borders, are associated with changes in color, irritation, ulceration, or bleeding (Fig. 1) (Albert and Jakobiec 2008; Esmaeli et al. 2003; Shields and Shields 2008; Vaziri et al. 2002).



Melanoma of the Eyelid, Fig. 1 Pigmented melanoma of the right lower eyelid

Diagnostics

A biopsy is necessary to make a definitive diagnosis. Biopsy should be considered for pigmented lesions exhibiting changes in size, color, or shape.

Differential Diagnosis

Differential Diagnosis includes ▶ melanocytic nevus, ▶ pigmented basal cell carcinoma, ▶ seborrheic keratosis, ▶ apocrine hidrocystoma, and ▶ varix.

Prophylaxis

Avoidance of sun exposure, use of sunscreens, sunglasses, and hats

Therapy

Wide surgical excision with adequate margins (at least 5 mm) and assessment for the presence of detectable metastatic disease along with short- and long-term follow-up is standard. Other treatments include radiation, cryotherapy, chemotherapy, and immunotherapy.

Prognosis

The prognosis and metastatic potential are related to the level of invasion of the dermis (depth) and the tumor thickness. Nodular melanoma has a vertical growth with early involvement of the dermis, therefore has a worse prognosis (Albert and Jakobiec 2008; Esmaeli et al. 2003; Shields and Shields 2008; Vaziri et al. 2002).

Epidemiology

1% of all malignant neoplasms of the eyelid skin.

Cross-References

- ▶ Basal Cell Carcinoma of Eyelid
- ▶ Hidrocystoma, Apocrine
- ▶ Seborrheic keratosis

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Melanomas of the Conjunctiva

- ▶ Melanomas, Conjunctival

Melanomas, Conjunctival

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Synonyms

Melanomas of the conjunctiva

Definition

Melanocytes normally reside in the basal layer (stratum basale) of the epithelium but can also be found in the subepithelial tissues in some conditions. Conjunctival melanoma is a malignant, neoplastic proliferation of atypical melanocytes that generally starts in the basal layer of conjunctival epithelium, penetrates the underlying epithelial basement membrane, and invades the subepithelial connective tissue.

Etiology

Mutation of the BRAF gene, a gene that encodes a serine/threonine kinase in the mitogen-activated protein kinase (MAPK) pathway, can lead to development of conjunctival melanomas. The MAPK pathway is involved in signal transduction, and dysregulation of the MAPK pathway in turn leads to abnormal cellular proliferation (Kenawy et al. 2013). Other genetic alterations have been implicated in the pathogenesis of conjunctival melanoma, but the significances and details of these abnormalities remain to be fully elucidated.

Clinical Presentation

A classic conjunctival melanoma presents as a unilateral, single, nodular, pigmented lesion on the bulbar conjunctiva at or near the limbus. However, it can also arise at the plica semilunaris or caruncle and be multifocal or nonpigmented. The edges can be discrete, diffuse, or mixed, and corneal involvement may result from direct extension from the limbus. Invasions of the orbit, nasolacrimal duct, and sinuses by conjunctival melanomas have also been reported. Around 70% of conjunctival melanomas arise from preexisting primary acquired melanosis (PAM); less commonly, they can arise from preexisting nevi or de novo (Shields et al. 2011).

Diagnosis

Diagnosis is made by biopsy, showing atypical melanocytes undergoing neoplastic proliferation and invading the subepithelial connective tissue. Immunohistochemical markers for melanocytic cells exist. They include MITF,

Melan-A, HMB-45, and S100. None of them are 100% sensitive or specific, so a combination of these markers, together with morphological features, is often required for diagnosis (Lim et al. 2013). Clinically, conjunctival melanomas are staged according to the tumor-node-metastasis (TNM) staging system developed by the American Joint Committee on Cancer (AJCC) and Union for International Cancer Control (UICC).

Differential Diagnosis

1. Hypermelanosis, such as freckle.
2. Secondary melanosis, such as Addison's disease.
3. Congenital ocular melanocytosis.
4. Other conjunctival malignancy, such as pigmented squamous cell carcinoma.

Therapy

Initial treatment for localized disease usually consists of surgical en bloc excisional biopsy to remove all macroscopic tumors. Incisional biopsies should be avoided if possible to minimize chance of tumor seeding. Surgical excision alone, without adjuvant therapy, has been shown to carry a higher risk for recurrence. Frequently, following surgical excision, some forms of adjuvant therapies are applied, such as topical alcohol, cryotherapy, brachytherapy, and topical mitomycin C. Other less common adjuvant therapies, such as carbon dioxide laser and topical interferon alpha 2b, have also been used (Lim et al. 2013). More extensive local disease or persistent recurrence may require exenteration. The role of sentinel lymph node biopsy remains controversial, but may be beneficial in patients with tumors thicker than 2 mm or non-limbal tumors, both of which seem to carry a higher risk for systemic metastasis (Lim et al. 2013). Metastatic disease is treated similarly to metastatic cutaneous melanoma, with systemic immunotherapy, targeted therapy, chemotherapy, or a combination of the aforementioned modalities.

Prognosis

The estimated 5-year mortality rate is 12–19%, whereas the 10-year mortality rate is around 30% (Kenawy et al. 2013). Patients with melanoma arising from PAM or nevus demonstrate better survival than those with melanoma arising de novo (Shields et al. 2011). Local tumor recurrence happens in 36–62% of cases (Lim et al. 2013). Risk factors for local recurrence include: multifocal disease, non-limbal position of the tumor, involvement of the surgical margins, and surgical excision without adjuvant treatment. The frequency of regional lymph node metastases is between 26% and 40%, although not all metastatic disease is preceded by regional lymph node metastases (Lim et al. 2013). Risk factors for metastatic disease include local disease recurrence, tumor thickness of more than 2 mm, and involvement of the non-bulbar conjunctiva, medial bulbar conjunctiva, caruncle, and plica semilunaris. Systemic disease most commonly involves the lungs, brain, liver, skin, bones, and gastrointestinal tract (Kenawy et al. 2013).

Epidemiology

Conjunctival melanoma constitutes about 2–5% of all ocular malignancies and 5–7% of all ocular melanomas. It is the second most common malignant neoplasm of the conjunctiva after squamous cell carcinoma. It has an incidence of 0.2–0.8 per million individuals per year in the Caucasian population, with only rare cases being reported in non-Caucasians (Kenawy et al. 2013). It may have a higher incidence in males, but the data is not conclusive. The median age of diagnosis is around 60 years old.

Cross-References

▶ Choroidal and/or Ciliary Body and/or Iris Melanoma

- ▶ Compound Nevus
- ▶ Conjunctival Nevus
- ▶ Primary Acquired Melanosis

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Melanosis

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Synonyms

Conjunctival epithelial melanosis; Conjunctival melanosis

Definition

Melanosis refers to excessive melanin production and retention of pigment by epithelial melanocytes. This process, however, does not elevate the surface of the conjunctiva. Nevi usually will cause elevation of the surface (Krachmer et al. 2011; Shields and Shields 2008).

Etiology

Exposure to ultraviolet light, inflammation, trauma, various hormones, toxic, genetic (Krachmer et al. 2011).

Occurrence

Unknown.

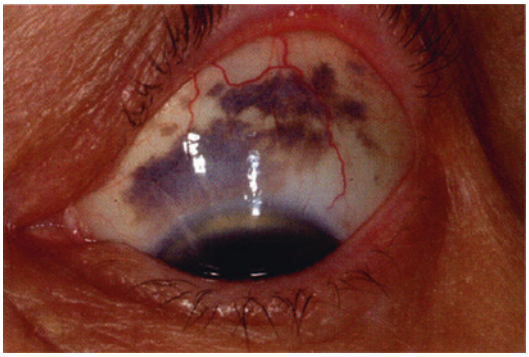
Classification

Classification of conjunctival melanosis is based on three main characteristics (Krachmer et al. 2011; Shields and Shields 2008):

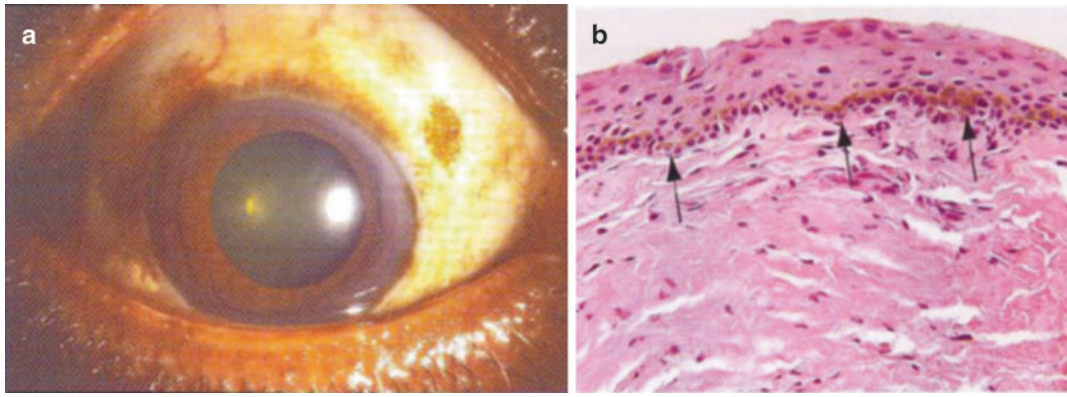
Benign or premalignant
Congenital or acquired
Epithelial or subepithelial
Primary or secondary

Based on the above, melanosis of the conjunctiva could be divided to (Krachmer et al. 2011; Shields and Shields 2008; Rosa and Harocopos et al. 2011):

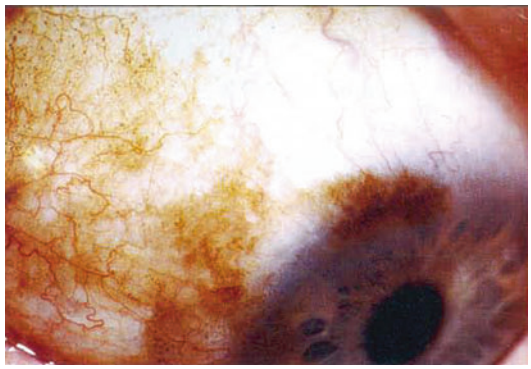
1. Epithelial congenital melanosis
   An ephelis (freckle) is a discrete, stationary lesion (present since birth or early childhood) characterized by excessive melanin production in the base of the epithelium by a normal number of melanocytes. This lesion is not a precursor of malignant melanoma.
2. Subepithelial congenital melanosis
   Subepithelial congenital melanosis is not a lesion of the conjunctiva but the episclera. Ocular melanocytosis or melanosis oculi is pigment change limited to tissues of the eye (Fig. 1).



Melanosis, Fig. 1 Melanocytosis



Melanosis, Fig. 2 Benign acquired melanosis (BAM). (**a**) Clinical appearance. (**b**) Histology shows a proliferation of melanocytes confined to the basal layer of the epithelium (*arrows*). The melanocytes are small, with no cellular atypia



Melanosis, Fig. 3 PAM (primary acquired melanosis)

In addition to increased numbers of pigmented melanocytes in the sclera and episclera, this condition is characterized by a congenital increase in the number, size, and degree of pigmentation of melanocytes of the uvea.

3. Secondary acquired melanosis
   The most frequent form is the acquired melanosis of the limbal and perilimbal conjunctival epithelium with irregular margins. It is also named BAM (benign acquired melanosis) (Fig. 2)
4. Primary acquired melanosis
   Primary acquired melanosis (PAM) is a neoplastic proliferation with potential for malignant transformation of melanocytes within the conjunctival epithelium (Fig. 3).

Cross-References

- ▶ Choroidal and/or Ciliary Body and/or Iris Melanoma
- ▶ Melanocytosis
- ▶ Primary Acquired Melanosis

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Melanosis Oculi

- ▶ Blue Nevus

Melasma

- ▶ Chloasma, of Eyelids
- ▶ Melasma, of Eyelids

Melasma, of Eyelids

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Synonyms

Chloasma; Melasma

Definition

A diffuse skin hyperpigmentation that is sometimes associated with pregnancy or the use of oral contraceptives.

Etiology

Thought to be related to female hormonal activity; however, the exact mechanism is unknown. Sun exposure also plays a significant role in precipitating its development. It has been reported in families as an autosomal dominant trait, and it has also been associated with eczema, rosacea, and other inflammatory skin disorders (Grimes 1995).

Clinical Presentation

Diffuse hyperpigmentation of the eyelids and may involve other areas of the face.

Diagnostics

Workup is usually not necessary.

Differential Diagnosis

Addison's disease
Lupus erythematosus
Lichen planus

Prophylaxis

Avoidance of sunlight may prevent exacerbation of melasma.

Therapy

Superficial chemical peels and topical depigmentation agents, such as hydroquinone, have been used to improve the cosmetic appearance of melasma (Grimes 1995).

Prognosis

Good; however, resolution of pigmentation with treatment is very gradual and sometimes suboptimal (Grimes 1995).

Epidemiology

More common in females, during pregnancy or with the use of oral contraceptives.

Cross-References

▶ Ephelis
▶ Lentigo Senile (Liver Spots)

References

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Meretoja Syndrome

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Synonyms

AGel amyloidosis; Amyloidosis V; Familial Amyloidosis, Finnish type; Hereditary gelsolin amyloidosis; Kymenlaakso syndrome; Lattice corneal dystrophy, gelsolin type; Lattice corneal dystrophy type 2; Primary hereditary systemic amyloidosis

Definition

Meretoja syndrome, or Lattice corneal dystrophy type 2, is a hereditary systemic amyloidosis that presents with lattice lines in the peripheral cornea.

Etiology

A mutation in gelsolin at chromosome 9q32-34 results in protein misfolding and formation of beta sheets in place of alpha helices. It is autosomal dominant with penetrance of 100%. Amyloid is deposited in fibrillar patterns throughout multiple organs, including the cornea in which lattice lines are present; these linear deposits are secondary to local production of amyloid in the cornea. Neuropathy with associated decrease in corneal sensitivity and facial nerve function is also secondary to amyloidosis.

Clinical Presentation

Patients classically present with lattice-like lines as an early sign. Linear amyloid deposits are present in the anterior to middle stroma and distributed peripherally, in contrast to lattice corneal dystrophy, which is paracentral and maintains a clear peripheral perilimbal cornea. Amyloid deposits between the epithelial basement membrane and Bowman's layer are consistent with all forms of lattice dystrophy, but amyloid deposits directly posterior to an intact Bowman's layer are characteristic for Meretoja syndrome. Involvement of the trigeminal and facial nerve results in dry eyes, reduced corneal sensitivity, diminished blink reflex, paralytic ectropion, blepharochalasis, and decreased contraction of orbicularis muscle. Secondary chronic open-angle glaucoma and cataract are common comorbidities.

Diagnosis

Clinical evidence of lattice lines by slit-lamp biomicroscopy with systemic amyloidosis is consistent with and generally diagnostic of Meretoja syndrome. Genetic analysis can be conducted to confirm mutation in the gelsolin gene. Histologically, amyloid deposits stain with periodic acid Schiff and Congo red and demonstrate apple-green birefringence under polarized light.

Differential Diagnosis

Multiple variants of lattice corneal dystrophy (LCD) have been described:

1. LCD 1 – no systemic association. Presents between 2 and 7 years of age
2. LCD 2 – Systemic amyloidosis
3. LCD 3 – no systemic association. Presents between 70 and 90 years of age

Prophylaxis

Amyloid deposition develops progressively, with no known method of prevention. Corneal haze is thought to increase proportionately with

intraocular pressure, and topical pressure-reducing eyedrops may assist in both reducing haze and decreasing risk of glaucoma.

Therapy

If limited to the anterior cornea, phototherapeutic keratectomy can remove or debulk deposits with improvement in visual acuity. Penetrating keratoplasty or deep anterior lamellar keratoplasty replaces diseased cornea with healthy donor tissue. However, these treatments all serve as temporizing measures, as amyloid deposition often returns after several years.

Prognosis

Patients lead a quality of life comparable to the general population, with vision typically unaffected until middle to older age. Lifespan is reduced secondary to systemic amyloidosis.

Epidemiology

Rare. First described by Meretoja in southern Finland, approximately 500 cases in the region have been documented; however, sporadic cases have been reported throughout the world.

Cross-References

- ▶ Corneal Dystrophies
- ▶ Lattice Dystrophy
- ▶ Lattice Lines
- ▶ Stromal Dystrophies

Further Reading

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Mesodermal Dysgenesis of the Cornea and Iris

▶ Axenfeld-Rieger Syndrome; Mesodermal Dysgenesis; Leukomas

Mesodermal Dysmorphodystrophy, Congenital

▶ Weill-Marchesani Syndrome

Metabolic Band Keratopathy

▶ Hypercalcemia: Corneal Changes

Metamorphopsia

▶ Monocular Distortion

Metastatic Endophthalmitis

▶ Bacteria, Endophthalmitis Caused by, Endogenous

Methanol Optic Neuropathy

▶ Methanol, Optic Neuropathy

Methanol, Optic Neuropathy

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Synonyms

Methanol optic neuropathy; Toxic optic neuropathy

Definition

Methanol is an odorless and colorless liquid found in many household and automotive products (e. g. antifreeze, windshield washer fluid, and copying fluid agents). Methanol intoxication leads to various forms of neurological impairments, one of which is a toxic optic neuropathy that could ultimately result in blindness. Ethylene glycol, a component of antifreeze, also can produce similar symptoms and toxic optic neuropathy to methanol.

Etiology

After ingestion, methanol enters the alcohol dehydrogenase pathway as a substrate and is metabolized to toxic metabolites, formic acid and formaldehyde. Humans have a limited ability to detoxify formic acid, which is a mitochondrial toxin that inhibits cytochrome oxidase (a mitochondrial enzyme), impairing mitochondrial functions. Since the optic nerve has a high energy demand and is especially susceptible to mitochondrial dysfunction, formic acid has been suggested to act as a mitochondrial toxin to the optic nerve and the retina. Methanol may more specifically affect the Muller cells, photoreceptors, and retrolaminar portion of the optic nerve.

Clinical Presentation

After the ingestion of methanol, patients typically present with acute signs of intoxication including abdominal pain, nausea, anion gap metabolic acidosis, vision loss, osmolar gap, and coma that often progress to death. The optic neuropathy is bilateral and typically severe and evolves rapidly, and toxicity may produce other visual symptoms including double vision, blurred vision, changes in color perception, photophobia, constricted visual field, and sometimes a total loss of vision to no light perception.

Diagnostics

The diagnosis of toxic optic neuropathies (such as those caused by methanol) is usually established by a detailed medical history and a complete eye examination. Blood testing for methanol levels may be performed in patients suspected of having methanol toxic neuropathy, but treatment should be initiated before the results return if possible in suspicious cases. Definitive diagnosis of methanol toxicity requires a confirmed increase in serum methanol level with gas chromatography (>20 mg/dl). Peak levels are

achieved 60–90 min after ingestion but do not correlate with the level of toxicity and thus are not a good prognostic indicator. Arterial pH seems to correlate best with formate levels (<7.2 is a severe intoxication).

A complete ocular examination should also be performed, including color vision and visual field testing. Visual field examination, static (Humphrey) or kinetic (Goldmann), is essential in evaluating any patient suspected of having toxic or nutritional optic neuropathy but may not be available in the acute or emergency room setting. Central or cecocentral scotoma with preservation of peripheral field is characteristic. Visual field defects in toxic optic neuropathy tend to be bilateral and relatively symmetric.

Differential Diagnosis

Hereditary optic neuropathies, nutritional optic neuropathy, compressive lesions of the anterior visual pathways, inflammatory optic neuropathies, infiltrative optic neuropathies, or bilateral traumatic optic neuropathy

Prophylaxis

Avoid ingestion of methanol-containing substances. Securing methanol products away from children may reduce poisonings.

Therapy

Treatment is targeted at inhibiting methanol metabolism, managing metabolic acidosis, and enhancing the elimination of toxic metabolites. In the past, ethanol could be administered to prevent further generation of toxic metabolites but safer alternatives exist now. Fomepizole is a potent ADH inhibitor and has largely replaced antidotal ethanol use for methanol toxicity.

Administration of intravenous sodium bicarbonate can correct the metabolic acidosis, and administration of intravenous folinic can enhance formic acid metabolism. Hemodialysis can also be utilized for clearance of methanol and formate.

Hemodialysis should be considered in ethylene glycol poisoning for patients with severe metabolic acidosis (pH 7.3), serum ethylene glycol level 50 mg/dL, and acute kidney injury. Finally, high-dose intravenous steroids may be beneficial when there is a short interval between consumption and treatment.

Prognosis

Some studies have shown that there is good outcome in blurred vision, but the prognosis of blindness was unpredictable. Visual loss is often severe and occasionally irreversible leading to optic nerve atrophy. It appears that the severity of acidosis at presentation is a key factor in determining the final visual acuity, and while early treatment is recommended, it still may not significantly impact the final visual outcome.

Epidemiology

Methanol toxicity remains a common problem in many parts of the developing world, particularly among members of lower socioeconomic classes especially where illegal production of ethanol might be contaminated with methanol (including countries which nominally ban commercial alcohol sales or possession). In addition, accidental and non-accidental poisoning can produce methanol or ethylene glycol toxicity. Toxic optic neuropathies in general are usually associated with employee exposures in a workplace or ingestion of materials containing toxic substances such as methanol. Toxic optic neuropathies have no racial predilection and are found equally in males and females. Any age may be affected. Toxic-nutritional optic neuropathy from ethanol is likely nutritional in origin, but discontinuing ethanol use is recommended.

Cross-References

- ▶ Optic Neuropathy
- ▶ Toxic Optic Neuropathy

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Meyer-Schwickerath Syndrome

- ▶ Cryptophthalmos-Syndactyly (Fraser) Syndrome

Microcornea

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Definition

Microcornea refers to a cornea with a horizontal diameter of less than 10–11 mm (Gupta and Kim 2010). The term microcornea should be reserved for cases of small corneas in an otherwise normal globe. However, one will find the term microcornea used to describe an abnormally small cornea in the setting of nanophthalmos or microphthalmos. Nanophthalmos refers to an abnormally small, but normally organized, globe. Microphthalmos refers to a small and disorganized globe (Gupta and Kim 2010; Sugar 2004; Waheed and Azar 2005).

Etiology

Microcornea is a congenital abnormality. Overgrowth of the anterior tips of the optic cup during eye development has been proposed to result in a smaller than normal corneal size (Gupta and Kim 2010; Waheed and Azar 2005).

Clinical Presentation

Microcornea can occur as an isolated anomaly, or the entire eye may be smaller than normal, with or without disorganization of the eye anatomy. Eyes with microcornea are likely to be hyperopic because their corneas are relatively flat. However, other refractive errors are possible (Gupta and Kim 2010; Waheed and Azar 2005). Twenty percent of patients with microcornea develop open-angle glaucoma later in life (Waheed and Azar 2005). Others may be predisposed to angle-closure glaucoma, as patients with microcornea may have relatively shallow anterior chambers. Other ocular or systemic abnormalities may be associated with microcornea (Table 1) (Gupta and Kim 2010; Sugar 2004; Waheed and Azar 2005).

Microcornea, Table 1 Ocular and systemic associations of microcornea

Ocular associations
Aniridia
Autosomal dominant vitreoretinal choroidopathy
Axenfeld syndrome
Coloboma (uveal)
Congenital cataract
Corectopia
Corneal leukoma
Cornea plana
Glaucoma (closed-angle, infantile, open-angle, narrow-angle)
Hyperopia
Mesodermal angle remnants
Microblepharon
Microphakia
Nystagmus
Persistent fetal vasculature
Persistent pupillary membrane

(*continued*)

Microcornea, Table 1 (continued)

Posterior lenticonus
Retinal pigmentary changes
Retinopathy of prematurity
Rieger anomaly
Small orbit
Systemic associations
Agnathia
Alagille syndrome
Alport syndrome
Congenital toxoplasmosis
Cornelia de Lange syndrome
Carpenter syndrome
Cohen syndrome
Crouzon syndrome
De Grouchy syndrome (chromosome 18p deletion syndrome)
Ehlers-Danlos syndrome (type VI)
Fetal alcohol syndrome
Goldenhar syndrome
Goltz syndrome (focal dermal hypoplasia)
Greig hypertelorism (Greig cephalopolysyndactyly syndrome)
Hallermann-Streiff syndrome
Kohn-Romano syndrome (blepharophimosis, ptosis, and epicanthus inversus)
MMCAT syndrome (microcornea, myopic chorioretinal atrophy, telecanthus, and posteriorly rotated ears)
Meckel syndrome
Meyer-Schwickerath syndrome (oculodentodigital dysplasia)
Micro syndrome (microcornea, congenital cataract, mental retardation, retinal dystrophy, optic atrophy, hypogenitalism, and microcephaly)
Nail-patella syndrome (onychoosteodysplasia)
Nance-Horan syndrome (X-linked cataract-dental syndrome)
Norrie disease
Partial deletion of chromosome 18q
Progeria
Rieger syndrome
Rubella
Sjögren-Larsson syndrome
Smith-Lemli-Opitz syndrome
Smith-Magenis syndrome
Trisomies 3p, 13, 18
Turner syndrome
Waardenburg syndrome
Weill-Marchesani syndrome
Weyers syndrome

Diagnosis

The diagnosis of microcornea is made by measuring the horizontal corneal diameter, which can be accomplished using a ruler, caliper, or with topography or biometry machines that measure the white-to-white distance. Slit-lamp examination, gonioscopy, and ultrasonography can help to differentiate simple microcornea from nanophthalmos and microphthalmos.

Differential Diagnosis

Cornea plana, sclerocornea, nanophthalmos, microphthalmos.

Therapy

Supportive measures include refractive correction and treatment of any associated glaucoma.

Prognosis

If microcornea is an isolated finding, the prognosis is generally good with refractive correction and treatment of any amblyopia (Gupta and Kim 2010). In pediatric patients undergoing cataract surgery, microcornea was associated with an increased risk of developing postoperative glaucoma (Rabiah 2004).

Epidemiology

Microcornea is a rare occurrence. Most cases of microcornea are sporadic, although autosomal dominant and autosomal recessive inheritance patterns have been described, particularly in association with syndromes (Khan 2012). For instance, an autosomal dominant inheritance pattern is found in families with congenital cataract – microcornea syndrome. Patients with the "micro" syndrome inherit microcornea, congenital cataract, mental retardation, retinal dystrophy, optic atrophy, hypogenitalism, and microcephaly in an autosomal recessive inheritance pattern.

Cross-References

- ▶ Corneal Diameter
- ▶ Nanophthalmos
- ▶ Microphthalmos (Microphthalmia)

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Microcystic Edema

- ▶ Bulla

Microcystic Epitheliopathy

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Synonyms

Corneal epithelial cysts; Epithelial microcystic edema

Definition

Condition in which the epithelium develops microcysts in response to acute or chronic stimuli.

Etiology

The formation of microcysts in the corneal epithelium occurs when edema appears within or between the cells with debris-filled cystic spaces formed during epithelial maturation (Krachmer et al. 2011).

Usually, the microcysts are small, typically 10–50 μm in size, with translucent irregular shape and high refractive inclusions, which form in the basal layer of the epithelium and move toward the anterior surface of the cornea. The cysts diameter can reach up to 900 μm depending on the disease (Keay et al. 2001).

The principal causes of cysts formation are:

1. Hypoxia: it leads to depletion of glycogen stores and a gradual decline in oxygen consumption with an increase in lactate accumulation. Intracellular edema indicates that epithelial compensatory abilities are surpassed. Microcysts are the easiest and the most distinctive form to detect corneal hypoxia (Keay et al. 2001; Krachmer et al. 2011).
2. Endothelial dysfunction: epithelial edema is caused by fluid elevating cells from the basement membrane producing a blister-like bullae appear. Desmosomal connections maintain epithelial integrity at this point. There are many grades of edema ending in large dome-shaped elevations in the epithelium (Bron and Tripathi 1973; Keay et al. 2001).
3. Changes in epithelium maturation: epithelial cells in rapid multiplication or degeneration result in formation of cysts due to accumulation of cells (Krachmer et al. 2011).

Occurrence

To identify the cysts formation in the corneal epithelial, a 16× magnification with

retro-illumination should be used to scan the cornea with 1 mm wide slit at an angle of 45° to the microscope. Depending on the etiology of the cyst, size, shape, and content may differ. Microcysts do not produce corneal staining, but when a great amount (>200) approach the corneal surface, areas of fluorescein staining called "negative staining" can be seen with a cobalt blue illumination and a yellow filter (Keay et al. 2001; Krachmer et al. 2011).

When the microcystic changes affect the visual axis, blurred vision may occur as a result of the irregular astigmatism caused by the faintly elevated corneal epithelium, as well as due to light diffraction and scattering. Occasionally, there is foreign body sensation. If the epithelial surface breaks or becomes loose and shifts during blinking, pain can occur. Meanwhile, many patients remain asymptomatic during long periods of time if any of the reported conditions do not occur (Keay et al. 2001; Smolin and Thoft 2005; Krachmer et al. 2011).

The most common cause for microcystic epitheliopathy occurrence is the contact lens-induced hypoxia. Trauma due to improper fitting or overwear and hypercapnia can also contribute to microcystic development. The number of microcysts increases as the oxygen transmissibility of the lens decreases and with longer overnight extended wear (Keay et al. 2001; Krachmer et al. 2011).

Other relevant causes of epithelial cysts are corneal dystrophies, such as Meesmann's and epithelial basement membrane dystrophy. The first presents within the first few months of life with intraepithelial microcysts, consisting of degenerated epithelial cell products due to rapid cell multiplication. The latter, also known as map-dot-fingerprint dystrophy, occurs in adults and appears with cysts (dots or Cogan's microcysts) beneath the basement membrane or within the epithelial layer alone, containing cellular and nuclear debris from cell degeneration (Smolin and Thoft 2005; Krachmer et al. 2011).

Edema caused by endothelial dysfunction leads to a condition called hydrokeratopathy or bullous keratopathy. As described before, there are many levels of edema in this pathology, and cysts commonly appear in the chronic edematous epithelium. Toxic stimulus to the epithelium leads to acute epithelial microcystic edema, which can be reversed after appropriate treatment. Recurrent erosions can also manifest with cystic formation in the edematous epithelium bordering the defect. This usually indicates defective epithelium and anticipates an episode of erosion. Cysts have been described as well in association with virus keratitis, pannus, and disorders that affect the tear film integrity (Keay et al. 2001; Smolin and Thoft 2005).

Classification

The epithelium can be affected focally or diffusely, depending on the etiology and stage of the disease.

Cross-References

- ▶ Corneal Dystrophies
- ▶ Endothelial Failure
- ▶ Epithelial Dystrophies
- ▶ Epithelial Erosions
- ▶ Epitheliopathy
- ▶ Map-Dot-Fingerprint Dystrophy (Epithelial/Anterior Membrane Dystrophy)
- ▶ Meesmann Dystrophy

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Microcystoid Degeneration – Cystic Retinal Tuft

► Retinal Peripheral Degeneration

Microkeratome

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Definition

The microkeratome is a surgical device with an oscillating blade that is used to create a predetermined thickness corneal flap during laser in situ keratomileusis. The flaps created with this instrument have a thickness of 100–200 μm.

Epidemiology

When in 2007 the number of femtosecond and microkeratome LASIK procedures was nearly 1:1, the microkeratome will probably become less used due to higher precision and faster methods.

History

Jose Barraquer developed the first microkeratome in the 1950s for use in lamellar refractive surgery. About 30 years later, Luis A. Ruiz modified the device and was able to create a flap of corneal tissue.

Clinical Features

Microkeratomes consist of two pieces, a suction ring for fixation and the flexible head with an oscillating blade. Currently, there are three main microkeratomes on the market, Carriazo–Barraquer (Microtech, Doylestown, PA), the M2 of Moria (Moria Surgical, Antony, France), and the Bausch & Lomb/Chiron Hansatome. Each one of these has a motorized rotating head to create the flap.

Tests

Thorough slit-lamp examination of the eyes and keratometric, keratographic, and pachymetric readings are required for preoperative planning to assure the best possible results.

Differential Diagnosis

Other procedures for creating corneal flaps are:

– Femtosecond laser

Etiology

See History section above.

Treatment

After topical anesthesia, the suction ring is brought into the right position. The microkeratome is then fixed onto the suction ring. During suction, visual acuity is lost due to high pressure and compression of the optic nerve. After making the flap, the suction ring and microkeratome are removed and the excimer laser procedure is started.

Cross-References

► Excimer Lasers
► Femtosecond Laser

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Micropannus

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Synonyms

Corneal neovascularization; Corneal vascularization

Definition

Micropannus is a form of subepithelial corneal fibrovascular proliferation, which extends beyond the normal vascular arcade at the limbus. Micropannus is differentiated from gross pannus in that its extension is less than 2 mm beyond the vascular arcade, while gross pannus goes beyond 2 mm. Micropannus is associated with many ocular surface disorders and can progress to frank scarring of the ocular surface as well as gross corneal neovascularization (NV). In rare instances it can progress to deep corneal neovascularization affecting the deeper stromal layers of the cornea.

Etiology

Micropannus generally develops as a result of four main processes:

1. Hypoxia. This is most commonly associated with extended contact lens wear, especially softgel contact lenses worn during sleep, as the lens and closed eyelid generate a barrier to corneal oxygenation. The development of neovascularization in this circumstance is an attempt by the cornea to manufacture an alternative source of oxygen supply to the cornea through the blood. Any long-term use of contact lenses will often result in the formation of micropannus. Silicon hydrogels appear to induce fewer hypoxic complications than softgel lenses (Martin 2007).
2. Irritation. Inflammation from allergic limbitis, vernal conjunctivitis, or chronic conjunctivitis can trigger the biochemical cascade of cytokines and other mediators resulting in the formation of pannus (Ellenberg et al. 2010; Chang et al. 2012).
3. Infection. Untreated chlamydial keratoconjunctivitis (inclusion conjunctivitis and trachoma) and staphylococcal blepharoconjunctivitis are common infectious causes, though any chronic infectious process can also trigger inflammation with resultant development of pannus from the mechanism described above (Jones 1975).
4. Aniridia. Patients with aniridia have a chronic keratopathy associated with abnormal limbal stem cells leading to conjunctivalization of the corneal epithelium. Aniridia leads to a complete absence of the palisades of Vogt, causing the epithelium to invade the cornea with resultant neovascularization. This results in gross pannus, but in early stages may appear as micropannus (Akpek et al. 2007).

Occurrence

Corneal vascularization is estimated to affect up to 1.4 million people per year. The incidence of corneal angiogenesis as a result of softgel lenses has been estimated to be between 18.2 and 19.8 per 10,000 individuals.

Classification

Ocular surface disease, corneal disorder, limbal disease

Cross-References

▶ Chlamydia
▶ Pannus/Micropannus
▶ Vogt Lines, Keratoconus

References

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Microphthalmia

▶ Microphthalmos (Microphthalmia)
▶ Nanophthalmos

Microphthalmos

▶ Nanophthalmos

Microphthalmos (Microphthalmia)

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Synonyms

Microphthalmia; Nanophthalmos

Definition

An eye with an axial length more than two standard deviations smaller than the age-adjusted mean (<19 mm in a 1-year-old, <21 mm in an adult)

Etiology

Microphthalmos is a congenital malformation that occurs during embryologic development. It is the end product of an insult to the optic vesicle that results in either incomplete invagination or closure. Causes include infection, ionizing radiation, toxins, or genetic defects. Two main types have been described:

1. Simple: small eye with otherwise normal structure and function (*nanophthalmos*)
2. Complex: small eye associated with other ocular abnormalities

Microphthalmos can occur as an isolated trait or as part of a broader syndrome.

Clinical Presentation

Presentation of microphthalmia varies according to severity and co-existing ocular pathology, but most commonly includes complaints of small eyes, strabismus, poor vision, or leukocoria. The patient may also commonly present as a referral from pediatrics during work-up for associated syndromes. Microphthalmos may be unilateral or bilateral. The most frequently observed associated ocular abnormalities include cataract, coloboma, corneal clouding, microcornea, nystagmus, persistent hyperplastic primary vitreous, orbital cyst, and glaucoma. One variant, posterior microphthalmos, disproportionately affects the posterior segment and may present with a normal looking anterior segment.

Diagnostics

Both A and B scan ultrasonography are used to evaluate axial length as well as the anterior and posterior segments. If clinical presentation is unilateral, the fellow eye should be evaluated for occult disease. The examiner should look for associated abnormalities and consider magnetic resonance imaging if indicated by detection of optic nerve head abnormalities or orbital cysts. In addition, if findings are consistent with an associated

syndrome, referral to appropriate systemic subspecialists for further work-up is important.

Differential Diagnosis

Differential diagnosis includes anophthalmos, or complete absence of ocular structures. Extreme microphthalmos may clinically resemble anophthalmos. The differential diagnosis of diseases associated with microphthalmos is large and includes trisomy 13, congenital rubella syndrome, congenital CMV, fetal alcohol syndrome as well as less common entities such as *m*icrophthalmia with *l*inear *s*kin defects (MLS) syndrome, *mi*crophthalmos, *d*ermal *a*plasia, and *s*clerocornea (MIDAS) syndrome, Waardenburg syndrome, Hurler syndrome, Goltz-Gorlin syndrome, and Hallermann-Streiff syndrome.

Prophylaxis

Avoidance of risk factors or prevention through rubella vaccination and minimization of fetal exposure to excessive alcohol or ionizing radiation. Referral for genetic counseling in appropriate cases

Therapy

Treatment varies according to associated abnormalities; however, effective surgical intervention in microphthalmic eyes is very difficult and often produces disappointing results. Systemic disease must be addressed by the appropriate subspecialists.

Prognosis

Prognosis is highly variable depending on associated ocular and systemic abnormalities. Microphthalmos with cyst, coloboma, or microcornea tends to have the poorest prognoses. Microphthalmic eyes without other abnormalities tend to be highly hyperopic and often develop angle-closure glaucoma later in life.

Epidemiology

Like anophthalmos, microphthalmos is rare, occurring in approximately 10–19 per 100,000 live births. It is often part of a syndrome the phenotypic presentations of which can vary greatly in severity.

Cross-References

- ▶ Axial Length
- ▶ Cryptophthalmos
- ▶ Cryptophthalmos-Syndactyly (Fraser) Syndrome
- ▶ Microcornea
- ▶ Nanophthalmos
- ▶ Orbit, Inflammation of

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Microphthalmos (Microphthalmia), Anterior

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Synonyms

Anterior chamber dysgenesis; Anterior segment dysgenesis; Complex microphthalmia; Microphthalmos with anterior segment dysgenesis

Definition

Microphthalmia refers to a globe that has a total axial length of less than two standard deviations below the mean for the age of the person. Anterior microphthalmia refers to a small eye with a small anterior segment length secondary to a deficit in embryological development of one of more component of the anterior segment of the eye. This is also referred to as complex microphthalmia with anterior segment dysgenesis.

Etiology

Various conditions involving the anterior aspect of eye can lead to shortened axial length. Anterior segment dysgenesis is one of the main causes behind anterior microphthalmos. Various tissues can be affected, including the cornea, iris, and the lens. The anomalies result principally from a defect in the migration of embryonic cells during the development of the eye. The anomaly can be unilateral or bilateral. It can also be an isolated finding, or associated with other malformations. It can also be sporadic or hereditary. Heritable causes can be from chromosomal defects or part of various syndromes.

Clinical Presentation

Anterior microphthalmia presents as an anterior segment length, the distance between the cornea and the back of the lens, that is two standard deviations below the mean for age. Anterior segment dysgenesis, a main cause of anterior microphthalmia, stems from numerous developmental abnormalities. These developmental abnormalities affect the cornea, iris, or ciliary body. There are few described anomalies of the anterior chamber, the main ones being Axenfeld-Rieger anomaly (displaced Schwalbe's line with bands of iris tissue bridging the iridocorneal angle, combined with a spectrum of defects of the iris and pupil), Peters anomaly (circumscribed opacification of the central cornea), and sclerocornea (opacity and vascularization of the cornea).

Diagnosis

The diagnosis of microphthalmia (anterior) is based on clinical and imaging studies. The physical exam consists mainly of detecting abnormalities in various structures of the eyes, as well as measuring corneal diameter. Imaging studies consist of A-scan to measure the axial length of the orbit, B-scan to evaluate internal structures, and MRI/CT to assess for size and structures of the orbits and surrounding structures.

Differential Diagnosis

The main differential diagnosis for anterior microphthalmia is distinguishing it from microcornea. On the other hand, anterior microphthalmia can be associated with various conditions that should be considered wherever the diagnosis is ascertained. The syndromic presentations include microphthalmia with linear skin defects, also known as MIDAS (microphthalmia, dermal aplasia, and sclerocornea), and Gazali-Temple syndrome. Cardiac defects also tend to be present in these syndromic microphthalmia.

Prophylaxis

Causes of microphthalmia may be sporadic or heritable. Prophylaxis consists mainly of avoid prenatal exposures to teratogens, specially alcohol, thalidomide, retinoic acid, and hydantoin. For heritable causes, prophylaxis consists of genetic counseling, along with the above measures.

Therapy

The extent of microphthalmia will dictate the best therapy course. Isolated cases will have

different management scenes than complex cases with associated craniofacial malformations. Surgery is the mainstay for severe microphthalmia and consultation with an oculoplastic surgeons advised.

Prognosis

Prognosis depends on the extent of the abnormalities. Anterior microphthalmia is usually associated with angle closure glaucoma.

Epidemiology

The exact prevalence of anterior microphthalmia is unknown. However, the prevalence of anophthalmia/microphthalmia is less than 1 per 10,000 birth.

Cross-References

- ▶ Microcornea
- ▶ Microphthalmos
- ▶ Nanophthalmos

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Microphthalmos with Anterior Segment Dysgenesis

- ▶ Microphthalmos (Microphthalmia), Anterior

Micropsia

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Synonyms

Accommodative micropsia; Psychogenic micropsia

Definition

Micropsia is a dysmetropsia (visual illusion) in which objects appear smaller than they are in reality. They are commonly associated with convergence or accommodation of a distance closer than that of the object viewed.

Etiology

The causes for micropsia include optical distortion (e.g., corneal or retinal disease including retinal edema, and macular degeneration) or by brain lesions (e.g., ischemic, neoplastic, or other occipital lesions).

Diagnostics

Patients with micropsia should first undergo evaluation of the eye as retinal causes are the most common. Amsler grid testing might be useful for documenting the laterality, size, location, and extent of the micropsia. Electroencephalogram (EEG) testing or neuroimaging might be necessary for possible intracranial etiologies especially if the ocular exam is normal and the findings are bilateral or hemianopic.

Therapy

Treatment of micropsia should be directed at the underlying condition.

Cross-References

▶ Macropsia
▶ Metamorphopsia

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Microulcerative Peripheral Keratitis

▶ Catarrhal (Marginal Corneal) Infiltrates

Midface Lift

▶ Cheek Elevation, in Eyelid Repair

Miescher-Melkersson-Rosenthal Syndrome

▶ Rosenthal Syndrome

Migraine with Benign Episodic Unilateral Mydriasis

▶ Benign Episodic Pupillary Mydriasis

Mild Head Trauma

▶ Concussive Trauma

Mild Traumatic Brain Injury (MTBI)

▶ Concussive Trauma

Milia

▶ Epidermal Cysts, of the Eyelid

Miller Fisher

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Synonyms

Fisher's syndrome

Definition

The Miller Fisher syndrome (MFS) is characterized by the clinical triad of ataxia, ophthalmoplegia, and areflexia. MFS was first described in 1956 by Miller Fisher as an unusual variant of Guillain-Barre syndrome (GBS) due to its similar cerebrospinal fluid profile and association with *Campylobacter jejuni*. Some authors believe that MFS may be a form of brainstem encephalitis due to the presence in some patients of abnormal electroencephalogram (EEG) findings, multiple cranial nerve palsies, and/or sensory disturbances (Asbury et al. 1995; Fenichel 2005).

Etiology

While the exact etiology of MFS is not clearly defined, many cases occur after a recent viral or bacterial infection, while others follow vaccination. A genetic predisposition (HLA-B39) in association with MFS has also been reported (Darras 2015).

Clinical Presentation

Clinically, MFS often initially presents with febrile illness or viral symptoms 5–10 days before the onset of neurological symptoms. The sequential cascade of ocular motor disturbances (often a paralysis of upgaze, then loss of lateral gaze, followed by loss of downgaze typically within a span of 2–3 days). Loss of tendon reflexes and decreased peripheral sensory input typically occurs 3–4 days after paralysis of eye muscles has reached maximum severity. Abnormal muscle coordination, generalized muscle weakness, ptosis, eyelid retraction, optic neuritis, and migratory paresthesias may also be noted. Some patients may have unilateral or bilateral facial paralysis (Leigh and Zee 1999).

Diagnosis

The diagnosis of MFS is a clinical one characterized by the classic triad of symptoms confirmed by lumbar puncture, electromyogram (EMG), and neuroimaging studies (Miller et al. 2005; Darras 2015).

Differential Diagnosis

The differential diagnosis of MFS includes Bickerstaff encephalitis, GBS with ophthalmoplegia, brainstem lesions, neuromuscular transmission disorders, and metabolic disorders.

Therapy

Treatment, in severe cases, is identical to that for GBS including plasmapheresis and intravenous immunoglobulin (IVIG) (Fenichel 2005).

Prognosis

Prognosis for the MFS is generally benign, but careful observation is highly recommended to monitor the progression of muscle weakness or the onset of respiratory failure. Recovery generally begins 2–4 weeks after symptoms manifest and reaching completion within 6 months, usually with no residual neurological deficits.

Epidemiology

Most patients with MFS are in mid to late adulthood, although children and infants have also been reported to have developed the condition. Annual incidence is estimated at 1/1,000,000 (Darras 2015).

Cross-References

► Facial Diplegia, Guillain-Barré Syndrome

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MIM # 253200

► Maroteaux-Lamy Syndrome

Mineralocorticoids

► Corticosteroids, Use in Ophthalmology

Minimum Angle of Resolution/ Recognition (MAR)

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Synonyms

MAR; Minimum separable

Definition

One important aspect of vision is spatial resolution, i.e., the ability to recognize differences of luminance between dark and bright object structures. This ability is proportional to the angle between the two structures or objects and the fovea. The angle at which two objects such as two points or two periods of a grating are just perceived as separate is the minimum angle of resolution (MAR). Its logarithmic form (logMAR) is commonly used as a metric for visual acuity.

Cross-References

► ETDRS Visual Acuity Chart

Minimum Separable

► Minimum Angle of Resolution/Recognition (MAR)

Minor Closed Head Injury

► Concussive Trauma

Minus Cylinder Convention

► Minus Cylinder Form

Minus Cylinder Form

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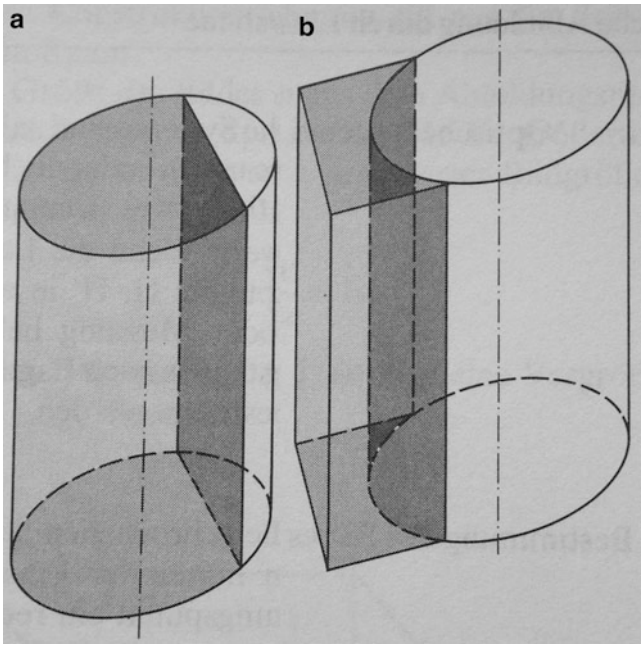
Synonyms

Minus cylinder convention

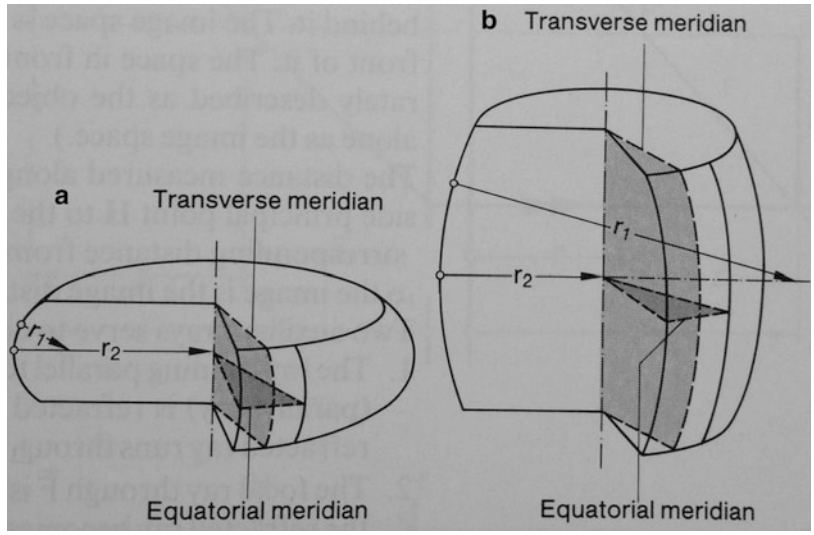
Definition

Lenses with at least one cylindrical, toroidal, or aspheric toroidal surface are not symmetrical to the optical axis and have a different power in each meridian plane. The rays are united in the two planes of the strongest and weakest refraction only. These two planes perpendicular to each other and are known as the principal meridians of the lens. Rays run in one of the meridian planes in front of the lens are at an angle toe each other after refraction (they no longer lie in one plane). For this reason the power of an astigmatic lens can only be measured in the two principal meridians and is given in the form of two equivalent powers or vertex powers F'_{v1} and F'_{v2}. The difference between the two principal powers is known as the astigmatic difference (cylinder): $C = F'_{v2} – F'_{v1}$. The formulae for all lenses with a spherical power apply for each of the two principal meridians. The simplest form of an astigmatic lens is a plano-cylinder (Fig. 1).

A toroidal surface is produced by rotation of a circular arc about an axis which does not run



Minus Cylinder Form, Fig. 1 Plano-cylindrical lenses: (**a**) positive, (**b**) negative



Minus Cylinder Form, Fig. 2 Toroidal Surfaces: (**a**) tyre-shaped, (**b**) barrel-shaped

through the center of this arc. The toroidal surface has different radii of curvature (r1 and r2 in Fig. 2) in the two principal meridians (transverse and equatorial meridians). In an aspheric toroidal (incorrectly, but common, atoroidal) surface, the transverse and equatorial meridians deviate from the circular shape.

Application: For the correction of astigmatic ametropia; also for anamorphic lens systems for motion pictures.

Further Reading

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Miosis

► Anisocoria of Small Pupil: Horner Syndrome
► Anisocoria of the Small Pupil

Misdirected Eyelashes

► Trichiasis

Mitochondrial Optic Neuropathy

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Synonyms

Dominant optic neuropathy (DOA); Leber hereditary optic neuropathy (LHON)

Definition

Mitochondrial optic neuropathy is defined as optic nerve damage in the setting of mitochondrial diseases. Mitochondria are important in cellular energy production, reactive species generation and scavenging, calcium regulation, and other functions to ensure cell integrity. The optic nerve is high in energy demand and is therefore especially susceptible to mitochondrial disease. Different types of mitochondrial optic neuropathies include hereditary optic neuropathies such as dominant optic atrophy (DOA), Leber hereditary optic neuropathy (LHON), and acquired optic neuropathies due to toxic damages to the mitochondria. This chapter will focus on hereditary mitochondrial neuropathies as specific types of toxic neuropathies are addressed in greater detail in other chapters.

Etiology

Mitochondrial optic neuropathies can be divided into hereditary (primary) and acquired (secondary) optic neuropathies. The underlying etiology of hereditary mitochondrial optic neuropathy is direct impairment of mitochondrial functions by either mitochondrial DNA or nuclear DNA. Two important types of mitochondrial optic neuropathies are DOA and LHON. In DOA, about 50% of the cases are due to a mutation in *OPA1* nuclear gene that encodes a dynamin-related GTPase known as OPA1 destined to be on the inner membrane of the mitochondrial cristae. Dysfunction of the OPA1 protein has been correlated to mitochondrial function abnormalities in mitochondrial fusion, oxidative phosphorylation, membrane stabilization, and mitochondrial DNA replication. Due to the high-energy demand nature of the optic nerve, it becomes especially susceptible to mitochondrial dysfunction.

On the other hand, LHON is due to mutations of mitochondrial DNA rather than nuclear DNA as seen in DOA. Three primary point mutations have been implicated in LHON that affects the function of mitochondrial respiratory chain complex I including G11778A, G3460A, and T14484C. Mutations in these genes have been implicated in decreased ATP production and increased free-radical production ultimately resulting in oxidative damage. The optic nerve is affected because of its high-energy demand and sensitivity to oxidative stress, with the most susceptible region being the unmyelinated axons within the papillomacular bundle while exiting the eye at the optic disk.

A rarer cause of hereditary optic neuropathy is a mutation in *OPA3* gene that presents as a multisystem disorder with hypotonia, optic atrophy, ataxia, cognitive impairment, and extrapyramidal signs.

Clinical Presentation

Both hereditary mitochondrial optic neuropathies are characterized by dyschromatopsia and central scotomas, reflecting the selective involvement of the papillomacular bundle. However, in DOA, the mean visual acuity at presentation is 20/80 to 20/120. Visual loss is usually seen in patients between ages 4 and 6 years, classically during vision screening at school. By age 11, the majority of DOA patients would have experienced some visual impairment. Neuroretinal rim thinning is common in DOA, and some patients may also present with peripapillary atrophy, "saucerization" of the disk, and a cup-to-disk ratio exceeding 0.5, mimicking glaucomatous cupping. The optic nerve also presents early with sectoral pallor. In about 20% of the patients with DOA, optic neuropathy may present as part of a syndromal disorder characterized by sensorineural hearing loss, peripheral neuropathy, myopathy, ataxia, ptosis, and/or ophthalmoplegia. These patients are considered to be DOA "plus" cases and often have greater optic nerve damage and worse visual acuities.

In LHON, visual loss is much more severe and is usually bilateral but in a sequential fashion over a period of time. Disease onset is characterized by painless acute loss of central vision with acuity usually worse than 20/200. About half of the patients have sequential visual loss, with the

interval between visual loss of two eyes ranging from 2 to 4 months, though it could be shorter or longer. The majority of patients will experience involvement of the second eye in less than a year. Pupillary light reflexes interestingly are sometimes preserved in patients, and funduscopic exams may reveal vascular tortuosity of central retinal vessels, circumpapillary telangiectatic microangiopathy, and swelling of the retinal nerve fiber layer. However, in about a fifth of the patients with LHON, the optic disk may look normal. In about 6 weeks, optic nerve pallor will become apparent.

Diagnostics

DOA is typically diagnosed during early childhood because of mild, bilateral, unexplained vision loss occurring in the context of a family history of DOA. Diagnostic tests such as optical coherence tomography (OCT) in patients with DOA disclose normal morphology of photoreceptor layer but a nonspecific thinning of the retinal nerve fiber layer. Dysfunction of the retinal ganglion cells and their axons is reflected in abnormal visual-evoked potentials and ERG. Identification of *OPA1* gene mutation in molecular testing also supports the diagnosis of DOA. Diagnosis of LHON includes identifying aforementioned clinical symptoms, as well as neuroimaging of the anterior visual pathway to rule out the possibility of other reversible causes. Molecular genetic testing can also aid in the diagnosis of LHON to detect the mitochondrial mutations, but most commercial laboratories only test for the three most common mutations (e.g., 11778, 14484, 3460).

Differential Diagnosis

Compressive optic neuropathies, inflammatory optic neuropathies, demyelinating optic neuropathies, ischemic optic neuropathies, metabolic optic neuropathies, toxic optic neuropathies, Wolfram syndrome, Costeff syndrome. We recommend consideration for neuroimaging (e.g., cranial MRI) in our patients with LHON.

Prophylaxis

Some studies have shown that smoking may be associated with visual loss in LHON, and others have shown a trend of heavy alcohol intake and visual failure. Therefore patients with LHON are strongly advised to not smoke as well as to moderate their alcohol intake. The role of treatment in asymptomatic carriers (e.g., idebenone) is controversial and unproven, but nonaffected LHON mutation carriers might choose to avoid mitochondrial environmental stressors (e.g., alcohol and tobacco).

Therapy

Treatments for mitochondrial optic neuropathy are limited as there has not been clear evidence to support the efficacy of any intervention. The primary focus for clinicians is to provide supportive measures such as low-vision aids and recognition and therapy of treatable systemic abnormalities. For patients with LHON, treatment with idebenone appears safe and reasonable, especially when given early in the course of their disease, but the drug is not approved for LHON in the United States or Europe. In addition, there have not been any proven DOA treatments, and the use of idebenone in DOA is still being investigated. On the other hand, gene therapy targeting retinal ganglion cells is a promising treatment option for patients with mitochondrial optic neuropathy.

Prognosis

In LHON, some patients may experience color vision and central visual acuity improvement in 6–12 months after visual loss onset. However, a more sudden return of vision characterized as "fenestration" within a central visual field defect could return years after symptom onset. The most important prognostic factor is the type of DNA mutation. The most common mutation 11778 along with mutation 3460 only has 4–22% chance of recovery, while the 14484 mutation has a 37–71% chance of visual recovery. Additionally,

age of onset less than 20 years (especially less than 10 years) is also a possible positive prognostic feature for better visual outcome. There have also been reports that thicker peripapillary retinal nerve fiber layer and large optic-disk vertical diameters may also be positive prognostic factors for LHON. In DOA, worsening of the visual field is insidious but constant and may be quantified as a loss of one Snellen line of acuity about every 10 years. Substantial spontaneous improvement is not common in DOA.

Epidemiology

Visual acuity in DOA typically decreases in the first two decades, and as mentioned previously, about half of the patients have a mutation in the *OPA1* gene. An additional gene identified in DOA patient is *OPA3* gene. DOA prevalence worldwide is estimated to be about 3 out of 100,000 individuals. Penetrance of DOA is at about 70% but can vary. On the other hand, LHON has been linked to multiple mutations of mitochondrial DNA, mainly G11778A, T14484C, and G3460A that comprise 95% of the LHON cases. The prevalence of LHON is estimated to be about 1 in 25,000 in Europe. Males are more commonly affected, and females tend to develop LHON later in life but may be more severely affected.

Cross-References

▶ Leber Hereditary Optic Neuropathy
▶ Optic Atrophy

Further Reading

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Mitochondrial-Related Retinal Degenerations (MRDs)

▶ DNA, Disorders with Retinal Phenotype, Associated with Mitochondrial DNA (mt-DNA) Mutations

Mitomycin C

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Synonyms

MMC

Definition

Antibiotic which was isolated from *Streptococcus caespitosus* in the 1950s. As it has cross-linking properties, it can bind DNA and prevent replication.

Indication

Mitomycin C is used in glaucoma filtering surgery and is able to avoid haze after surface ablation of the cornea as well as in treatment for existing haze. Studies have also shown that it is also useful in the prevention of pterygium.

Contraindication

Wound complications can occur when mitomycin C is used in patients with Sjogren's syndrome, dry eye, meibomian gland dysfunction, neurotrophic keratitis, herples simplex keratitis, as well as

myelosuppression, pregnancy, lactation, and diverse coagulation disorders.

Use and Dosage

The concentrations used vary from 0.04% to 0.1%. See "Indication" section above.

Adverse Reactions

Nausea, vomiting, anorexia, anemia, alopecia, fever, paraesthesia, pneumonia, dyspnea, malaise, pruritus, extravasation, bladder fibrosis, myelosuppression, hemolytic-uremic syndrome. There are reports of scleral necrosis, thin bleb, leaking bleb, infection, and hypotonia in patients who were operated for glaucoma or pterygium.

Interactions

No drug interactions are known for mitomycin C.

Cross-References

- ▶ PRK
- ▶ Pterygium

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MMC

- ▶ Mitomycin C

Mohs'

- ▶ Mohs' Micrographic Surgery

Mohs' Micrographic Surgery

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Synonyms

Mohs'; Mohs' surgery; Mohs' technique

Definition

An excisional technique developed by Dr Frederic Mohs in 1933. Characterized by the progressive removal of tumor combined with microscopic examination of the removed tissue in order to thoroughly map the tumor margins and the excision site (Nesi et al. 1998; Albert et al. 1999; Nerad 2001; Albert and Jakobiec 2008).

Indication

Conventionally, Mohs' surgery has been used to remove squamous and basal cell carcinomas. However, other types of carcinomas and skin tumors have been excised with Mohs' technique.

Contraindication

Although not an absolute contraindication, Mohs' technique is not recommended for the removal of

melanomas, sebaceous cell carcinoma, or other aggressive malignancies that histologic analysis may be difficult with rapid frozen sectioning.

Techniques and Principle

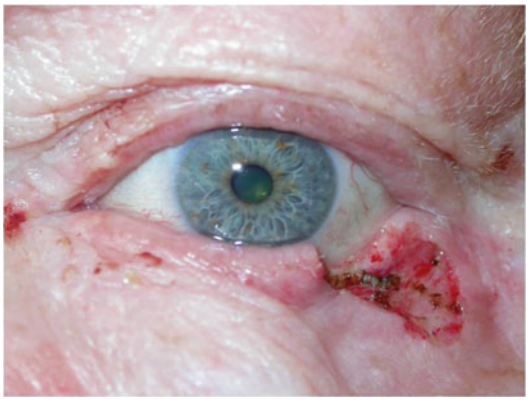
Mohs' surgery is usually performed as an outpatient procedure. First, the tumor is briefly debulked. Tissue is then removed layer by layer; the tissue was examined immediately after removal utilizing frozen sections. Sometimes curettage of the area of the lesion is performed to bring out the margins as normal skin responds differently to curettage than the abnormal cells. After the removal of a layer, the specimen is divided into sections (usually two sections) and marked with dyes. This provides a detailed map of the specimen. The margins of the specimen are then identified. If any of the margins are clear, the surgeon removes more tissue only from the suspected areas that still contain malignant cells, leaving the areas that have clear margins alone. The process is repeated until the whole lesion has been mapped and removed (Fig. 1).

Outcome

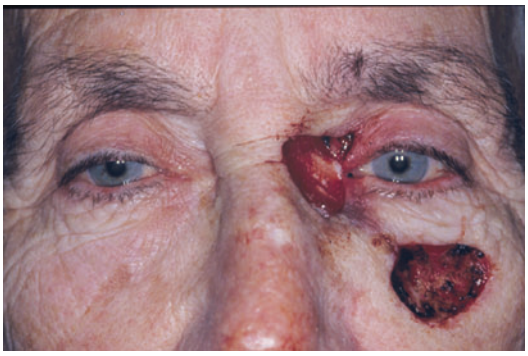
Mohs' technique is intended to preserve more normal tissue surrounding a malignancy. The preservation of essential structures around the eyelids may yield improved function and aesthetic outcomes. Mohs also allows for complete removal of the tumor conferring a high cure rate for certain skin carcinomas.

Complications

Mohs' surgery requires highly specialized equipment and a Mohs' trained surgeon in order to avoid tissue processing errors. The surgery is also lengthy in time, as the tumor is removed microscopic layer by microscopic layer, which may raise the risk for infection. Additionally, complex closure may necessitate the expertise of a specialist surgeon and thus a need for a second surgery (Fig. 2).



Mohs' Micrographic Surgery, Fig. 1 The final stage of Mohs' surgery for an eyelid skin tumor



Mohs' Micrographic Surgery, Fig. 2 Patient after Mohs' surgery ready for reconstructive surgery of the medial canthus and malar area

Cross-References

- Basal Cell Carcinoma of Eyelid
- Choroidal and/or Ciliary Body and/or Iris Melanoma
- Squamous Cell Carcinoma of Eyelid

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Nesi FA, Lisman RD, Levine MR (1998) Smith's ophthalmic plastic and reconstructive surgery, vol 31, 2nd edn. Mosby, St. Louis, pp 609–635

Mohs' Surgery

► Mohs' Micrographic Surgery

Mohs' Technique

► Mohs' Micrographic Surgery

Moll's Cyst

► Sweat Glands of Eyelid, Tumors Arising in

Molluscum Contagiosum

► Epidermal Cysts, of the Eyelid

Molluscum Contagiosum, of Eyelid

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Synonyms

Epithelioma contagiosum

Definition

Molluscum contagiosum (MC) is a viral infection (family Poxviridae) that can affect the eyelid.

Etiology

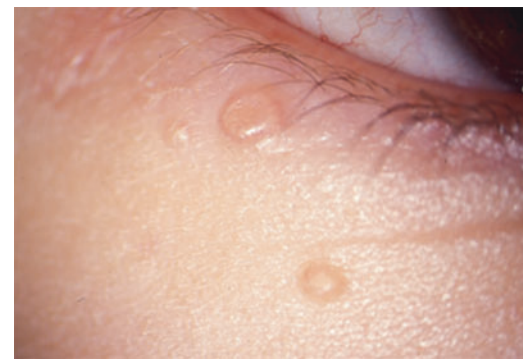
MC lesions are produced by a large DNA poxvirus that is usually transmitted by direct contact or fomites in children and by sexual activity in adults. Multiple lesion formation from autoinoculation is common (Charteris et al. 1995; Albert and Jakobiec 2008; Shields and Shields 2008).

Clinical Presentation

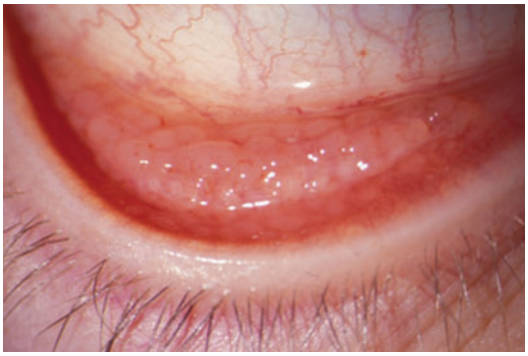
Lesions are typically pale, round, raised, painless skin papules with umbilicated centers, each measuring 3–6 mm (Fig. 1). Some may be as large as 3 cm and more aggressive, especially in immunosuppressed patients (HIV). They are frequently located near the lid margin and conjunctiva and may be associated with a follicular conjunctivitis and corneal changes (superior micropannus and fine epithelial keratitis) (Fig. 2) (Charteris et al. 1995; Albert and Jakobiec 2008; Shields and Shields 2008).

Diagnostics

Clinical, based on the typical appearance of the lesion and histopathologic confirmation.



Molluscum Contagiosum, of Eyelid, Fig. 1 Multiple lower lid lesions with central umbilication



Molluscum Contagiosum, of Eyelid, Fig. 2 Follicular reaction, inferior tarsal conjunctiva

Differential Diagnosis

Differential diagnosis includes ▶ verruca vulgaris, ▶ epidermal cysts, fibromas, ▶ basal cell carcinoma, ▶ squamous cell papilloma, ▶ keratoacanthoma, ▶ milia, and nevus.

Prophylaxis

Avoid skin-to-skin contact with others in order to prevent transmission and avoid scratching to prevent autoinoculation.

Therapy

Treatment is not always mandatory; the local immune response to infection may be sufficient to eliminate the virus and produce regression of the molluscum nodule in many cases. Sometimes, a more aggressive approach may be necessary to arrest symptoms, prevent transmission, and prevent corneal damage. Excision or cryotherapy are the most common interventions (Charteris et al. 1995; Albert and Jakobiec 2008; Shields and Shields 2008).

Prognosis

Excellent, except in the immunocompromised (such as HIV) in which the clinical picture may present as multiple widespread, persistent, disfiguring lesions, especially on the face (Charteris et al. 1995; Albert and Jakobiec 2008; Shields and Shields 2008).

Epidemiology

Uncertain, but commonly seen in healthy individuals or the immunosuppressed.

Cross-References

- ▶ Basal Cell Carcinoma of Eyelid
- ▶ Epidermal Cysts, of the Eyelid
- ▶ Keratoacanthoma
- ▶ Milia
- ▶ Squamous Cell Papillomas of Eyelid
- ▶ Verruca Vulgaris

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Molluscum Contagiosum: Overview

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Synonyms

Dimple wart; Epithelioma contagiosum

Definition

Molluscum contagiosum (MC) is a poxvirus that causes bengin and self-limiting round papular lesions on the skin and mucous membranes, including the lid margins, skin of the lids, and the brow (Schornack et al. 2006).

Etiology

MC skin eruptions are induced by a poxvirus that is transmitted by direct skin-to-skin contact or through fomite (Schornack et al. 2006; Cherry et al. 2009). It can also spread by autoinoculation through scratching and rubbing of one's lesion (Riordan-Eva and Cunningham 2011).

Clinical Presentation

Infecton of the eyelid may be unilateral or bilateral. Eyelid nodules tend to be isolated with mild surrounding inflammation, ranging from 1 to 3 mm in diameter (Schornack et al. 2006; Riordan-Eva and Cunningham 2011). Older lesions can have central indentation with a white or waxy-appearing core (Schornack et al. 2006; Riordan-Eva and Cunningham 2011). The lesions can be larger and more widespread in human immunodeficiency virus (HIV) infected and other immunocompromised individuals (Cherry et al. 2009). Nodules on the lid margin, skin of the lid, and brow may result in unilateral chronic follicular conjunctivitis, superior keratitis, and superior pannus resembling trachoma (Schornack et al. 2006).

Diagnosis

MC is usually diagnosed clinically by the characteristic appearance of the skin lesion (Schornack et al. 2006). Biopsy can confirm the clinical diagnosis (Schornack et al. 2006). Histology shows eosinophilic inclusions that fill the entire cytoplasm of enlarged cells with their nucleus pushed to the side (Schornack et al. 2006).

Differential Diagnosis

Flat warts, pyogenic granuloma, skin lesions due to cryptococcosis, histoplasmosis or *Penicillium marneffei* infection, basal cell carcinoma, amelanotic melanoma, milia, nevus.

Prophylaxis

Avoid direct contact with contaminated fomite and skin-to-skin contact with infected individuals (Riordan-Eva and Cunningham 2011). Cover the skin lesions to prevent autoinoculation and transmission to others (Riordan-Eva and Cunningham 2011).

Therapy

A Cochrane Review of treatment for MC recommends MC lesions to be left to heal naturally since no mechanimcal treatment (e.g., cryotherapy) and medical treatment (e.g., 1% imiquimod cream) have been found to be effective (van der Wouden et al. 2009). Patients with HIV may see improvement in MC skin lesions after initiation of antiretroviral therapy (van der Wouden et al. 2009).

Prognosis

The infection is self-limited. In immunocompetent individuals, the lesions usually resolve within 2 months and have complete clearance of infection within few months (Schornack et al. 2006). But in immunocompromised invidiuals, the infection may persists for a few years (Schornack et al. 2006).

Epidemiology

MC primary affects children. Children between 0 and 14 years have the highest incidence, ranging from 12 to 14 episodes per 1,000 children per year (Olsen et al. 2013). There was an increased incidence in adults in the 1980s due to the acquired immune deficiency syndrome (AIDS) epidemic (Olsen et al. 2013). The number of adult cases has decreased since the use of highly active antiretroviral therapy (HAART) (Olsen et al. 2013).

Cross-References

- ▶ Basal Cell Carcinoma of Eyelid
- ▶ Follicular Conjunctivitis
- ▶ Keratitis
- ▶ Molluscum Contagiosum, of Eyelid
- ▶ Pannus/Micropannus
- ▶ Pyogenic Granuloma

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Molluscum Sebaceum

- ▶ Keratoacanthoma

Monoclonal Antibody

- ▶ Antivascular Endothelial Growth Factor

Monocular Bobbing

- ▶ Ocular Bobbing

Monocular Diplopia

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Synonyms

Ghost image; Shadow image

Definition

The subjective perception of seeing an object twice with one eye. Monocular diplopia typically occurs when the ocular point spread function has two maxima that are apart enough from each other to be perceived as two separate points. Therefore, monocular diplopia is almost exclusively a consequence of ▶ optical aberrations. Typical conditions that cause monocular diplopia are uncorrected ▶ corneal astigmatism (dominant aberration: ▶ astigmatism), ▶ dry eye syndrome, ▶ corneal dystrophies, corneal scars, ▶ keratoconus, and early ▶ cataract (dominant aberration: ▶ coma). Higher-order aberrations of higher frequency such as trefoil and tetrafoil can also cause polyopia that is perceived as multiple images of a single object, often if point-shaped light sources are viewed. Also a double pupil aperture (polycoria), e.g., after iridodialysis or iridectomy can cause monocular diplopia.

In clinical practice, it is imperative that patients who complain about "double vision" undergo a careful anamnesis to differentiate between monocular and binocular diplopia. While monocular diplopia persists if one eye is covered, binocular diplopia disappears. Moreover, monocular diplopia is often reported as a "shadow," "ghost image," or a "second outline" of an object. Besides optical aberrations, also neurological causes are possible. However, cerebral diplopia or polyopia is extremely rare.

Cross-References

- ▶ Astigmatism
- ▶ Keratoconus

Monocular Distortion

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Synonyms

Metamorphopsia

Definition

Monocular distortion is the subjective phenomenon of seeing an object distorted. The underlying causes are multiple. The clinically most important one is also referred to as metamorphopsia (MMO). MMO is the subjective perception of straight objects such as lines appearing distorted or bent. Typically, an uneven macular architecture due to ▶ edema, ▶ drusen, epiretinal gliosis, or traction is the underlying pathology. Much more rarely, MMO is caused by aberrations such as very high-frequent ▶ coma resulting in local broadening of the point spread function. Optical aberrations such as uncorrected high astigmatism and high coma are more likely to cause a distortion of the point spread function along an axis. The corresponding perception is a distortion rendering objects "elongated" or "compressed" over a larger angle. A common and very simple test to detect MMO is the Amsler chart.

Monocular Polyopia

- ▶ Diplopia Monocular

Monocular Transient Visual Loss in Carotid Artery Disease

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Synonyms

Amaurosis fugax; Transient monocular vision loss (TMVL)

Definition

TMVL in carotid artery disease can be caused by hypoperfusion, thrombosis, or thromboembolic disease. This is usually due to progressive atherosclerotic internal carotid artery (ICA) stenosis, but vasculitis (e.g., giant cell arteritis) and arterial dissection are other mechanisms for disease. The thrombotic disease in the ICA however can lead to thromboemboli which can cause retinal or ocular ischemia leading to the TMVL. Significant stenosis of over 70% can also cause hypoperfusion ischemia. Activities such as postural change can decrease the perfusion pressure and retinal claudication may result from increased bright light exposure.

Diagnostics

Imaging of the head and neck (e.g., MRI) and the carotid arteries (e.g., MR angiography (MRA), computed tomography angiography (CTA), or carotid Doppler) might be diagnostic, but standard catheter angiography might still be needed in some cases.

Treatment

Treatment should be directed at the underlying etiology. Antiplatelet therapy might be indicated as medical treatment, and hemodynamically significant symptomatic ICA stenosis might require carotid angioplasty or stenting or surgical carotid endarterectomy. Carotid dissection may require medical or endovascular treatment. Vasculitis typically requires immunosuppressive therapy.

Cross-References

- ▶ Monocular Transient Visual Loss, Hypoperfusion Causing
- ▶ Monocular Transient, Visual Loss Embolic Causes of

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Monocular Transient Visual Loss, Hypoperfusion Causing

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Synonyms

Amaurosis fugax; Transient monocular vision loss (TMVL)

Definition

The ophthalmic artery (OA) provides the blood supply to the eye and orbit and the inner and outer retina as well as the optic nerve via the posterior ciliary arteries, cilioretinal arteries, central retinal artery or branch retinal arteries). Decreased blood flow in the ophthalmic artery or its branches may lead to hypoperfusion and result in transient monocular vision loss (TMVL) also known as amaurosis fugax. There are several potential causes of hypoperfusion including flow-limiting stenosis, vasculitis, hypovolemia, hypotension, anemia, arrhythmia, and thrombotic, embolic, or thromboembolic disease. Thus, the typical workup for amaurosis fugax (i.e., TMVL) often includes blood studies (e.g., CBC, platelet count, ESR, and C-reactive protein in elderly patients), echocardiogram, EKG, neuroimaging, and carotid imaging (e.g., carotid Doppler studies). TMVL may be exacerbated by decreased ocular perfusion (e.g., changes in posture or neck position) or retinal "claudication" from increased retinal oxygen demand (e.g., exposure to bright light). Postprandial TMVL has also been associated with vascular steal syndrome. Treatment revolves around correcting the underlying cause (e.g., correct anemia, treat vasculitis, address hemodynamically significant stenosis, antiplatelet, or anticoagulation therapy).

Cross-References

▶ Monocular Transient Visual Loss in Carotid Artery Disease

Further Reading

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Petzold A, Islam N, Hu H, Plante GT (2013) Embolic and nonembolic transient monocular visual field loss: a clinicopathologic review. Surv Ophthalmol 58(1):42–62

Monocular Transient Visual Loss, Ocular Causes of

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Synonyms

Amaurosis fugax; Transient monocular vision loss (TMVL)

Definition

There are several situations in which transient monocular vision loss (TMVL) can occur due to ocular causes. The specific signs and symptoms to look for include redness or injected conjunctiva, ocular pain, and tearing. Ocular surface etiologies for TMVL often report relief of symptoms with rubbing or blinking of the eye in question. Severe pain, halos around lights, tearing, redness, elevated intraocular pressure, and vision loss are suggestive of acute or intermittent angle-closure glaucoma.

Subluxation or dislocation of an intraocular lens (IOL); spontaneous, traumatic, or IOL-related hyphema (blood in the anterior chamber); intermittent anterior uveitis; or transient glaucoma can cause TMVL. Vitreous floaters or hemorrhage

can also cause TMVL. Congenital optic disk abnormalities, disk drusen, and papilledema are also associated with TMVL.

Cross-References

► Monocular Transient Visual Loss, Orbital Causes of

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Monocular Transient Visual Loss, Orbital Causes of

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Synonyms

Amaurosis fugax; Transient monocular vision loss (TMVL)

Definition

Orbital causes of transient monocular vision loss (TMVL) are uncommon. Orbital inflammation, orbital cellulitis, orbital neoplasms, and thyroid eye disease may all produce TMVL. One of the key symptoms of TMVL includes gaze-evoked amaurosis. In these cases, patients may complain of TMVL induced by gaze and caused by orbital lesions compressing the optic nerve in extremes of gaze.

Diagnostics

Orbital imaging (CT or MR) might show the lesion (e.g., optic nerve sheath meningioma, thyroid eye disease, orbital tumors).

Treatment should be directed at the underlying etiology.

Cross-References

► Diplopia in Graves' Ophthalmopathy
► Transient Monocular Vision Loss (TMVL)

Further Reading

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Monocular Transient Visual Loss, Stroke After

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Synonyms

Amaurosis fugax; Cerebrovascular accident (CVA); Transient monocular vision loss (TMVL)

Definition

If a patient has a stroke or cerebrovascular accident (CVA) and has a recent history of transient monocular vision loss (TMVL), the cause revolves around a vascular concern. CVAs may be hemorrhagic or ischemic. Cranial computed tomography (CT) or magnetic resonance imaging (MRI) can show the CVA. Embolic or thromboembolic CVAs are often preceded by TMVL. Ischemic TMVL thus serves as a warning sign, similar to a transient ischemic attack (TIA), of the potential for an impending CVA. Thrombosis, emboli, or thromboemboli can originate from uncontrolled atrial fibrillation, atherosclerosis in the carotid arteries, or vasculitides.

Diagnostics

Neuroimaging including diffusion-weighted imaging (DWI) on MRI, evaluation of the carotid arteries (e.g., carotid Doppler, MR angiography of neck, or CT angiography of the neck), cardiac evaluation (e.g., EKG, echocardiogram), and hematologic studies may be necessary in patients with TMVL and/or ischemic stroke related to TMVL.

Cross-References

▶ Cerebrovascular Accident (CVA)
▶ Monocular Transient Visual Loss in Carotid Artery Disease

References

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Monocular Transient Visual Loss, Systemic Causes of

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Synonyms

Amaurosis fugax; Transient monocular vision loss (TMVL)

Definition

Systemic causes of transient monocular vision loss (TMVL) can be separated into hypoperfusion, vasculitides, hypercoagulable or hyperviscosity states, and other systemic causes.

Giant-cell (temporal) arteritis is the most common vasculitis causing TMVL in the elderly. In younger patients, systemic lupus erythematosus, polyarteritis nodosa, granulomatosis with polyangiitis (formerly Wegener granulomatosis) and eosinophilic granulomatosis with polyangiitis (formerly Churg-Strauss syndrome), or other anti-neutrophil cytoplasmic antibody (ANCA)-related vasculitides may be the etiology. Hypercoagulable states include coagulation pathway deficiency states (e.g., protein S, protein C, or antithrombin III deficiency), genetic mutations (e.g., factor V Leiden or prothrombin 20210 mutation), antiphospholipid antibody syndrome (due to either lupus anticoagulant or anticardiolipin antibodies), or elevated plasma homocysteine. Hyperviscosity states caused by excess red blood cells (e.g., polycythemia vera), white blood cells (e.g., leukemia), platelets (e.g., thrombocytosis), or protein (e.g., multiple myeloma, Waldenstrom macroglobulinemia) can also lead to thrombosis and TMVL.

Treatment

Treatment should be directed at correcting the underlying etiology (e.g., vasculitis, hypercoagulable or hyperviscosity state).

Cross-References

- ▶ Giant Cell Arteritis
- ▶ Monocular Transient Visual Loss in Carotid Artery Disease

Further Reading

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Monocular Transient, Visual Loss Embolic Causes of

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Synonyms

Amaurosis fugax; Transient monocular vision loss (TMVL)

Definition

Embolic or thromboembolic causes of transient monocular vision loss (TMVL) can be due to atherosclerosis (mainly in the elderly), dissection of the carotid artery, cardiac thromboemboli formation (less common), or hypercoagulability (such as antiphospholipid antibody syndrome). Other less common causes of emboli include air, amniotic membrane, fat, and talc. Emboli usually

cause TMVL because of the temporary ischemia to the retina or optic nerve. Although most arterial emboli to the retina arise from the internal carotid artery, heart, or aorta, sometimes the external carotid artery is implicated (e.g., carotid stump syndrome). The emboli can sometimes be visualized on dilated fundus exam as refractile cholesterol bodies (e.g., Hollenhorst plaques), platelet thrombin complexes, or calcific emboli. Most patients with a possible embolic source for TMVL require carotid imaging such as ultrasound, neuroimaging (e.g., MRI with diffusion weighted imaging (DWI)), as well as head and neck vasculature imaging (e.g., CTA or MRA, carotid Doppler), EKG, and echocardiography.

Treatment

Treatment involves treating the underlying embolic source and may require anticoagulation and/or antiplatelet therapy. Some embolic sources require endovascular or surgical management.

Cross-References

▶ Monocular Transient Visual Loss in Carotid Artery Disease

Further Reading

Petzold A, Islam N, Hu H, Plante GT (2013) Embolic and nonembolic transient monocular visual field loss: a clinicopathologic review. Surv Ophthalmol 58(1):42–62

Mooren Ulcer

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Synonyms

Chronic serpiginous ulcer of the cornea

Definition

Mooren ulcer is a painful peripheral corneal ulceration occuring in the absence of any associated scleritis or any detectable systemic disease.

Etiology

Mooren ulcer has been casually related to different entities. Infectious causes, such as helminthiasis and hepatitis C, have been previously described (Schanzlin 1994). It was been postulated that the antigen-antobiody reaction to heminthic toxins within the cornea induced keratitis and inflammation (Schanzlin 1994). Also, other infectious associations such as herpes simplex, tuberculosis, and syphillis have been described in Mooren ulcer (Brown and Mondino 1984). Interestingly, Mooren ulcer has been reported following physicial trauma and foreign body injury, following cataract extraction and penetrating keratoplasty (Sangwan et al. 1997).

Occurrence

Mooren ulcer is rare and is usually seen in healthy adult males without any systemic disease. Nevertheless, Mooren ulcer can occur in either sex and at any age. There are two clinical types of Mooren ulcer: benign/unilateral and malignant/bilateral disease (Wilson et al. 1994). It was also found that 43% of older patients had bilateral disease, whereas bilateral disease was present in only one-third of patients below 35 years of age (Lewallen and Courtright 1990).

References

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Morning Glory Disc

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Synonyms

Morning glory disc anomaly; Morning glory syndrome

Definition

The morning glory disc anomaly (MGDA) is a rare congenital optic nerve head malformation eponymously named for its resemblance to the morning glory flower. When presenting in conjunction with commonly associated signs and symptoms, it can be referred to as morning glory syndrome (Kindler 1970).

Etiology

MGDA is believed to be an embryological defect in the development of the lamina cribrosa and the posterior sclera. Histopathological findings support this theory by the characteristic presence of glial tufts with hyaloid vascular components, suggesting a failure of fetal vasculature to regress. To date, no specific genetic defect has been consistently identified in patients with MGDA (Lee and Traboulsi 2008; Manschot 1990).

Clinical Presentation

MGDA patients are often initially referred to the ophthalmologist for strabismus or leukocoria as infants. Ninety percent of patients present with some form of strabismus. On fundus examination, the most defining characteristic of MGDA is an increased number of straight retinal vessels exiting an enlarged optic disc, with excavation of the optic nerve, in a vascular pattern that resembles radial spokes. Other common findings are central glial tufts, peripapillary pigmentation, and microphthalmia. Vision is impaired in the affected eye, with fewer than 30% of patients achieving a visual acuity of 20/40 or better. Macular involvement occurs in approximately 50% of patients. Thus, patients often have visual field defects and enlarged blind spots. Since MGDA is usually unilateral, relative afferent pupillary defects are also common (Lee and Traboulsi 2008).

MGDA has also been associated with several other systemic signs and symptoms: cleft lip, cleft palate, hypertelorism, basal encephalocele (most frequently transsphenoidal), agenesis of the corpus callosum, endocrine abnormalities involving the pituitary gland, Moyamoya disease, and facial capillary hemangiomas (Lee and Traboulsi 2008).

Diagnostics

MGDA is diagnosed on fundus examination, careful to differentiate from optic nerve coloboma and peripapillary staphyloma. Neuroimaging is recommended for MGDA.

Differential Diagnosis

It is critical that MGDA is not mistaken for optic nerve coloboma which is associated with systemic syndromes such as coloboma of the eye, heart defects, choanal atresia, growth retardation, genitourinary abnormalities, and ear abnormalities (CHARGE). Optic nerve coloboma is also a white excavation of the optic nerve; however, it preferentially affects the inferior portion of the nerve and can extend into the choroid and retina. In contrast to MGDA, optic nerve coloboma does not present with central glial tufts or radial retinal vasculature. Peripapillary staphyloma is another condition which is characterized by excavation of the optic disc; however, it lacks the radial retinal vasculature and central glial tufts which define MGDA (Lee and Traboulsi 2008).

Prophylaxis

None currently identified.

Therapy

There is currently no treatment for MGDA. However, accurate diagnosis and proper management is necessary to preserve remaining vision in the affected eye. Early treatment of amblyopia can help. Since MGDA is associated with an increased risk of retinal detachments of the posterior pole, with an incidence of approximately 33% over 10 years, dilated fundus exams should be used for detection. Brain imaging (MRI, MRA, CTA) should be performed to detect associated vascular and structural abnormalities (Lee and Traboulsi 2008).

Prognosis

MGDA is typically static but management of amblyopia and screening for retinal detachment are important. However, each of the associated systemic symptoms which can define morning glory disc syndrome (i.e., Moyamoya) carries its own prognosis and must be identified and treated early (Lee and Traboulsi 2008).

Epidemiology

MGDA is a rare condition which some sources state affects both men and women equally, while other sources state an incidence ratio of 2:1 (women-men) and a decreased risk in African-Americans (Lee and Traboulsi 2008; Brodsky 2010).

Cross-References

- ▶ Double Ring Sign: Optic Nerve Hypoplasia
- ▶ Off-Center Optics
- ▶ Optic Disc

References

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Morning Glory Disc Anomaly

▶ Morning Glory Disc

Morning Glory Syndrome

▶ Morning Glory Disc

Morquio Syndrome

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Synonyms

Morquio-Brailsford syndrome; MPS-IV; Mucopolysaccharidoses IV

Definition

Morquio syndrome is a lysosomal storage disease involving the failure to break down and therefore the deposition and accumulation of the glycosaminoglycan keratan sulfate in the body.

Etiology

Mucopolysaccharidoses (MPS) result in the accumulation of glycosaminoglycans (GAGs) secondary to the enzyme necessary to break down the GAG being either deficient or defective. Morquio syndrome has a more severe Type A and a more mild Type B form which are caused by the lack of two separate enzymes for each. Patients with Type A Morquio syndrome lack *N* -acetyl-galactosamine-6-sulfate sulfatase. This results in an accumulation of keratin sulfate and also chondroitin sulfate. Patients with the milder Type B Morquio syndrome lack the enzyme b-galactosidase which results in an accumulation of keratan sulfate. Morquio syndrome is inherited in an autosomal recessive pattern.

Clinical Presentation

Patients present primarily with severe skeletal abnormalities and little neurological dysfunction and have urinary excretion of keratan sulfate. Patients may present with the severe Type A form or the mild Type B form. Bone and joint involvement are common in both types. Skeletal manifestations appear in the first year of life and include joint laxity, genu valgum, and pectus carinatum. In addition to the joint laxity, patients may also have odontoid process hypoplasia which can result in atlantoaxial subluxation. This is of particular concern as patients often present with cervical spinal cord compression. Patients will have normal or near-normal intelligence, sensorineural deafness, abnormal facies, aortic valvular disease, and hepatosplenomegaly. They also present with dustlike corneal opacities throughout the corneal stroma. Keratan sulfate is already normally the most abundant GAG in the cornea, making up 65% of the total GAG content of the cornea. Typically, the corneal epithelium and endothelium appear normal.

As can be expected in a disease of accumulating GAGs, these dustlike corneal opacities can recur in patients who have corneal grafts. Retinal findings may be subtle and may only be seen in older patients. Patients with electroretinogram (ERG) abnormalities with or without pigmentary retinal degeneration or optic nerve atrophy have also been reported. Patients with Morquio syndrome present with short-trunk dwarfism, kyphoscoliosis with vertebral defects and spinal compression, and normal or near-normal intelligence.

Patients will usually have moderate corneal clouding by age 10. Patients may or may not have retinal pigmentary degeneration and often do have optic atrophy. However, unlike other mucopolysaccharidoses, Morquio syndrome is not associated with optic nerve swelling.

Diagnosis

Patients with Morquio syndrome will be found to have accumulation and urinary excretion of keratan sulfate. Patients can be screened by testing their urine for the specific GAG. Diagnosis can be made by WBC enzyme assay.

Differential Diagnosis

The differential diagnoses for Morquio syndrome include Hurler syndrome (MPS-I-H), Scheie syndrome (MPS-I-S), Hurler-Scheie compound (MPS – H/S) in which patients are heterozygote for both Hurler and Scheie syndromes, Hunter syndrome (MPS-II), Sanfilippo syndrome (MPS III), Maroteaux-Lamy syndrome (MPS-VI), Sly syndrome (MPS-VII), and Natowicz syndrome (MPS-IX).

Prophylaxis

As this is genetic disease, there is no prophylaxis to prevent getting this disease.

Therapy

Treatments for mucopolysaccharidoses have included bone marrow transplants in the past, but given issues with donor availability and significant donor availability, enzyme replacement therapy has now become the most common treatment for mucopolysacchridoses. In one of the enzymes that can be replaced, laronidase (a-L-iduronidase) has been shown to improve walking and lung function tests. Therefore it has been approved by the FDA for patients with Hurler syndrome or Hurler-Scheie syndrome. However, enzyme replacement therapy also has several limitations.

In additionally to being a very expensive treatment option, a significant drawback for enzyme replacement therapy is the inability to cross the blood-brain barrier. This significantly limits the ability to treat CNS and even ocular complications from these diseases.

Gene therapy may serve as an avenue for future therapy. In the treatment, viral vectors with the therapeutic gene used to incorporate into the host cells and produce the missing enzyme. In animal models of Hurler syndrome (MPS-I), improvements in ocular disease have been noted.

On a separate note, As Morquio syndrome has the combination of odontoid process hypoplasia and joint laxity resulting in atlantoaxial subluxation. Because of the very serious threat of cervical cord compression, posterior spinal fusions have been performed to prevent this.

Prognosis

Morquio syndrome is typically not recognized at birth. Patients tend to present with the disease around the second year of life. Most commonly this is through recognition of gait disturbances and delayed child growth.

Teenagers will advance through puberty normally or slightly later than their peers. The patient's fertility is also unaffected. Depending on the severity of the disease, cardiac or respiratory disease may cause death in the third or fourth decade of life.

Epidemiology

The estimated incidence of Morquio syndrome (MPS-IV) has a wide range, including 1 case per 263,157 births in Germany, 1 case per 200,000 births in British Columbia, and 1 case per 75,000 births in Northern Ireland. There is a 1:1 male to female ratio of patients with Morquio syndrome.

Cross-References

▶ Hurler-Scheie Syndrome
▶ Pseudo-Hurler Polydystrophy

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Morquio-Brailsford Syndrome

► Morquio Syndrome

Mosaic Degeneration (Anterior Crocodile Shagreen)

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Synonyms

Anterior crocodile shagreen; Secondary anterior crocodile shagreen of Vogt

Definition

Bilateral central corneal opacification manifesting as a mosaic of polygonal gray opacities separated by clear tissue at the level of Bowman's layer.

Etiology

Thought to be related to the oblique insertion of collagen lamellae in the corneal stroma (Tripathi and Bron 1975; Belliveau et al. 2009).

Clinical Presentation

Patients are asymptomatic and the findings are noted incidentally on routine slit lamp examination. Signs are bilateral, polygonal, gray-white opacities in the deep layers of the epithelium or in Bowman's layer (Vogt 1981).

Diagnostics

Clinical observation using slit lamp biomicroscopy is the standard for diagnosis. More recently, in vivo confocal microscopy has been used which demonstrates dark striae in the extracellular matrix and a mosaic pattern of the collagen lamellae (Woodward et al. 2007).

Differential Diagnosis

Differential diagnosis includes ► posterior crocodile shagreen (central cloudy corneal dystrophy of Francois). It is distinguished from this by its lack of inheritance pattern and its anterior stromal rather than posterior stromal involvement.

Therapy

Observation

Prognosis

Good prognosis without any associated progression or visual disturbance.

Epidemiology

Increasing prevalence in elderly patients, unknown incidence.

Cross-References

► Corneal Degenerations

References

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Motion Blindness

▶ Akinetopsia

MPS I-HS

▶ Hurler-Scheie Syndrome

MPS VI, MPS 6

▶ Maroteaux-Lamy Syndrome

MPS-IV

▶ Morquio Syndrome

MS

▶ Diplopia in Multiple Sclerosis

MS-Associated Uveitis

▶ Uveitis in Multiple Sclerosis

Mucopolysaccharidoses IV

▶ Morquio Syndrome

Mucopolysaccharidosis

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Definition

The mucopolysaccharidoses (MPS) are a group of autosomal-recessive metabolic diseases that are part of the larger group of lysosomal storage disorders. Mucopolysaccharidosis is estimated to affect 1 in 25,000 babies born in the United States (National Institute of Neurological Disorders and Stroke 2014). It is characterized by a deficiency of lysosomal enzymes that are required to break down glycosaminoglycans (GAGs), molecules that are found in the bone, cartilage, tendon, skin, and the eye. Without sufficient breakdown, glycosaminoglycans accumulate in the cells of connective tissues, thereby causing permanent, progressive cellular damage. These diseases can affect multiple organ systems, causing a combination of neurological deficits, developmental delay, seizures, skeletal irregularities, heart disease, hepatosplenomegaly, respiratory failure, and more. Most patients initially experience normal development and then a progressive decline in physical and/or mental function, eventually leading to premature death in severe cases. Ocular involvement in MPS is very common and has been described in all subtypes of MPS: the cornea, sclera, trabecular meshwork, retina, optic nerve, and posterior visual pathways can all be affected. Ocular manifestations include high hyperopia, corneal clouding, peripheral vascularization of the cornea, retinopathy, glaucoma, optic nerve edema, optic atrophy, progressive pseudoexophthalmos, hypertelorism, amblyopia, and

strabismus. These are all a result of intra- and extracellular GAG accumulation in ocular and periocular tissues and the brain. GAG accumulation in the cornea affects keratocyte size and upsets the regularity of the collagen fibril network in the corneal stroma, thereby clouding the cornea. Central corneal thickness is often within normal range. GAG deposition in trabeculocytes can cause outflow obstruction, high intraocular pressure, and resultant open-angle glaucoma and corneal edema. Narrow-angle glaucoma is theorized to occur from GAG accumulation in the peripheral cornea and other anterior segment structures, with or without ciliary body cysts. Falsely elevated intraocular pressure is probably a result of increased corneal rigidity and can lead to unnecessary pressure-lowering therapy. GAG accumulation occurs in the retinal pigment epithelium and the interphotoreceptor matrix, leading to a retinal dystrophy. Increased intracranial pressure can be a manifestation of MPS and lead to optic nerve swelling. Scleral thickening can impinge the optic nerve, and GAG accumulation in ganglion cells or in the optic nerve sheath can produce optic disk swelling and eventual optic atrophy. Hematopoietic stem cell transplantation is a treatment option for certain MPS patients but can give rise to graft-versus-host disease with its associated ocular surface issues. Enzyme replacement therapy is another treatment option but it is not available for all types of MPS. With respect to the different types of MPS, Hurler syndrome (MPS I H) and Maroteaux-Lamy syndrome (MPS VI) have the most severe corneal clouding. Retinopathy is most severe in Sanfilippo syndrome (MPS III). Corneal transplantation is a surgical therapeutic option to treat corneal clouding but recurrent opacification of the donor cornea has been reported. There is also evidence that systemic therapy with enzyme replacement therapy or hematopoietic stem cell transplantation can slow down or improve the progression of some ocular manifestations such as corneal clouding (Fahnehjelm et al. 2012).

References

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Mucopolysaccharidosis Type VI

▶ Maroteaux-Lamy Syndrome

Mucosal Graft

▶ Buccal Mucous Membrane Graft

Mucous Membrane Pemphigoid (MMP)

▶ Pemphigoid, Cicatricial

Mucus Fishing Syndrome

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Definition

Mucus fishing syndrome refers to chronic irritation of the ocular surface and is characterized by digital "fishing" of mucus strands from the inferior conjunctival fornices. Often initiated by dry eye symptoms, symptoms tend to worsen or recur with continuous manipulation. Treatment is conducted by education and avoidance of touching the eye in order to break a positive feedback cycle of abrasion and irritation.

Cross-References

- ▶ Allergic Conjunctivitis
- ▶ Dry Eye

Further Reading

McCulley JP, Moore MB, Matoba AY (1985) Mucus fishing syndrome. Ophthalmology 92:1262–1265

Mucus-Secreting Cells

- ▶ Goblet Cells, Mucin Tear Secretion by

Müller's Muscle

- ▶ Retractors, Lower Eyelid

Multifocal Intraocular Lens

- ▶ Apodized Diffractive Intraocular Lens

Multifocal Lenses

- ▶ Bifocal Lenses

Multiple Endocrine Neoplasia (MEN) 2B

- ▶ Sipple-Gorlin Syndrome, Enlarged Corneal Nerves

Multiple Recurrent Serosanguineous Retinal Pigment Epithelial Detachments in Black Women

- ▶ Polypoidal Choroidal Vasculopathy

Multiple Sclerosis Diagnosis

- ▶ Poser Criteria, for Multiple Sclerosis

Multipuncture Capsulotomy

- ▶ Can-Opener Technique

Munchausen Syndrome

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Synonyms

Artifactual illness; Deliberate disability; Hospital addiction syndrome; Surreptitious illness

Definition

Factitious disorder imposed on self (formerly Munchausen syndrome (MS)) or imposed on

others (formerly MS by proxy) is one of the most serious type of factitious disorders in which physical or psychological complaints are produced without an organic etiology in order for the patient to assume the sick role. This is different from malingering per se in that there is no clear secondary gain for the patient. Although the behavior is intentional, the underlying desire and need to secure the sick role is usually out of the patient's control. Even the risk of serious injury or death is not able to deter the patient from these behaviors. Physical symptoms may be completely fabricated, self-inflicted, or reflect genuine organic pathology resulting from intentional abuse or misuse of medications. Generally, their goal is to be admitted to the hospital to have further testing performed on them, and they will often resist being discharged. Many patients may have extensive diagnostic testing and even surgical procedures in an attempt to find the "underlying etiology." This syndrome may be more common in young, unmarried, and well-educated women but may occur in any age group, in either gender, and in any socioeconomic or educational class (Ferri 2015). Interestingly, MS occurs more commonly among those that work in health care, such as physician, nurses, or technicians. The patients commonly have extensive knowledge about medical terminology and may go into elaborate detail when relaying their history (Heer 2014). Some patients may exhibit objective physical exam findings which further complicates their diagnosis and necessitates a diagnostic work-up to rule out any organic cause since sometimes these patient will have medical problems (either self-induced or organic) which require intervention. Onset may occur after a psychological stressor, like the ending of a relationship, but it is generally unknown what causes an individual to begin this behavior (Ferri 2015). Such behavior often lasts for many years and patients may travel from hospital to hospital or city to city to continue their factitious disorder.

A related disorder is factitious disorder imposed on another (formerly known as Munchausen syndrome by proxy) in which a caretaker, unfortunately most commonly by the patient's own mother, simulates or produces an illness in the dependent so that they can vicariously assume the sick role through the dependent. In about a quarter of the cases, illness is simulated without producing any direct harm to the child, but in about half of the cases illness is actually be inflicted upon the child (poisoning, intentional misuse of medication, injection of infectious substance, etc.). This factitious disorder is considered a form of child abuse and should be treated appropriately (Heer 2014). A similar type of abuse may occur in elderly patients and their caretakers.

The American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM), Fifth Edition (DSM-5) classifies factitious disorder within the category of somatic symptom and related disorders. The large majority of factitious disorder patients show physical complaints and have the stated belief that they have a genuine medical illness. Munchausen syndrome by proxy was not formally named until 1977 and was only included in the DSM IV () and is now termed "factitious disorder imposed on another" in DSM V. The defining characteristics of all forms of factitious disorder are as follows:

- Intentional production of feigned physical or psychological signs or symptoms
- Presence of illness behavior reflecting a wish to assume the sick role
- Confronting physicians with self-induced symptoms or disease
- Absence of external incentives for the behavior (e.g., economic gain, avoiding legal responsibility, or improving general well-being) (Heer 2014)

In regards to ophthalmology, loss of visual acuity is the most common complaint of MS, but other common presenting symptoms might include loss of a visual field, transient loss of vision, visual illusions or hallucinations, diplopia, ptosis, blepharospasm, or photophobia (Bose 2008). It is important that when first seeing these patients that the physician remains objective in their evaluation, looking for organic causes for symptoms and identifying inconsistencies that suggest a nonorganic cause (Bose 2008).

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Mustarde Cheek Rotation Flap

► Mustarde Flap

Mustarde Flap

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Synonyms

Cheek rotation skin flap to the lower lid; Mustarde cheek rotation flap; Mustarde rotational cheek flap

Definition

Large rotational skin muscle flap used in the reconstruction of large defects of the lower eyelid.

Indication

The Mustarde flap is indicated for the reconstruction of large (greater than 50 %) full thickness lower eyelid defects. The flap provides a vascularized anterior lamellar flap. It preferred to eyelid sharing techniques for reconstruction of large lower eyelid defects in monocular patients, those with active corneal disease, and in children as it avoids prolonged eyelid closure during healing.

Contraindications

This technique is usually not indicated in lower eyelid defects involving less than 50 % of the eyelid margin or for the reconstruction of partial thickness defects. The skin of cheek/midface region, which will be advanced to fill the lower eyelid defect, should be healthy tissue.

Techniques and Principles

The lower eyelid defect is converted into a base-up triangle to allow for proper advancement and rotation of the flap without excess tissue bunching. The incision is extended laterally from the lateral canthus, extending in an upward fashion to the temporal region and then extending inferiorly in the preauricular area. The dissection plane of the flap is in the deep subcutaneous tissues. This ensures the flap is of appropriate thickness to optimize its viability while avoiding deeper dissection below the level of the SMAS and possible injury to the facial nerve branches. It is important to establish good vertical height for correct positioning of the lateral canthus. The posterior lamella defect is reconstructed with a posterior lamellar substitute such as nasal septum, free tarsoconjunctival graft, hard palate graft, or ear cartilage graft. The advanced Mustarde flap provides the vascularized tissue to allow for viability of the free posterior lamellar graft. The Mustarde flap is then closed with multiple deep sutures to remove tension from the closure and the skin is then closed with sutures. Depending on the degree of intraoperative bleeding, consideration can be given to placement of a drain, but this is usually not needed. Pressure dressing should however be placed over the flap to decrease the likelihood of postoperative hematoma formation.

Outcome

The mustarde flap provides a vascularized anterior lamellar flap for the reconstruction of large full thickness lower eyelid defects with a resultant scar which extends from the lateral canthus arching superiorly over the zygoma and continuing along the preauricular region. The resulting reconstructed lower eyelid is usually capable of providing adequate protection to the globe.

Complications

Lower eyelid malpositions including ectropion or entropion are possible. This can occur from contraction and fibrosis of the flap and is often exacerbated by the lack of orbicularis oculi muscle to provide stability to the reconstructed lower eyelid. The flap raised is large, and postoperative infection or hematoma formation can result in flap necrosis and tissue loss. The scar from the surgery is often obvious and difficult to camouflage. Care must be taken with proper dissection depth as to avoid injury to the branches of the facial nerve and resultant facial paralysis.

Cross-References

- ▶ Buccal Mucous Membrane Graft
- ▶ Canthal Reconstruction
- ▶ Cheek Elevation, in Eyelid Repair
- ▶ Eyelid Reconstruction
- ▶ Hard Palate Graft
- ▶ Semicircular Flap
- ▶ Simple Rotational Flap
- ▶ Transposition Flap

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Mustarde Rotational Cheek Flap

▶ Mustarde Flap

Mustarde Rotational Flap

▶ Rotational Flap for Eyelid Repair

Myasthenia Gravis, Overview

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Definition

Acquired myasthenia gravis (MG) is an autoimmune neuromuscular disease caused by autoantibodies directed against the postsynaptic acetylcholine (ACh) receptors and characterized

clinically by variability of function and abnormal fatigability of striated muscles.

Etiology

MG can be congenital or acquired. We will not be discussing the congenital or neonatal forms of MG. The acquired form is associated with autoantibodies directed against neuromuscular postsynaptic acetylcholine (ACh) receptors (i.e., binding, blocking, and modulating antibodies) that have a relationship with the thymus gland. These autoantibodies both accelerate the rate of degradation of ACh receptors and bind to the receptors, thereby decreasing the ability of acetylcholine to produce an effective depolarization on the postsynaptic neuron. In addition, the number of postsynaptic ACh receptors is decreased in MG patients, thereby causing the end-plate potential to be inadequate for generating contraction of some muscle fibers.

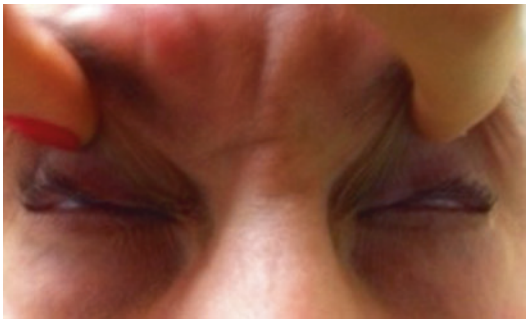
Clinical Presentation

Ocular symptoms, ptosis and diplopia, are present at onset in MG in approximately 70% of patients and are eventually present in 90% of patients. Patients with MG alone should not present with pain, proptosis, pupil involvement, paresthesia, or loss of vision because the disease only affects striated muscle and not sensory nerves or other organ systems. The ptosis in MG occurs due to the involvement of the levator palpebrae muscle and usually initially presents unilaterally but with eventual progression to bilateral involvement in many cases. The ptosis can be complete or incomplete, variable or intermittent, and unilateral, bilateral, or alternating. Likewise, the diplopia is also variable and fatigable with ophthalmoplegia in any pattern, and involvement of any one or combination of the extraocular muscles can occur in MG. Thus, MG can mimic the presentation of unilateral or bilateral, complete or incomplete ptosis; pupil-spared third, fourth, or sixth cranial nerve palsies; horizontal or vertical gaze palsy; internuclear ophthalmoplegia; chronic progressive external ophthalmoplegia; complete unilateral or bilateral complete ophthalmoplegia; or isolated extraocular muscle palsy (e.g., inferior oblique palsy). The patient may describe the ptosis as progressively worsening throughout the day (or better or even normal upon awakening), and the diplopia may be variable and fluctuating throughout the day. Nystagmus may occur because of muscle fatigue; however, nystagmus in isolation in MG is not typical. MG confined to the lid and extraocular muscles is called ocular MG, but generalized MG eventually develops in approximately 50–70% of patients, while 30–40% of patients remain purely ocular. In most cases, if generalization of ocular MG has not occurred in the first two years after diagnosis, it is less likely to occur.

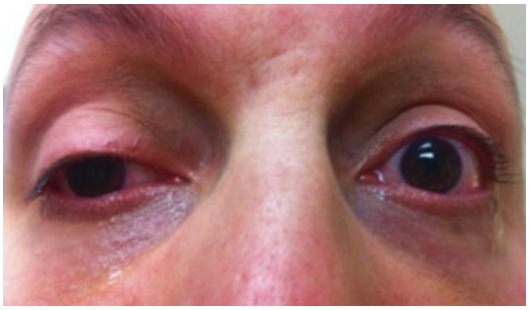
Diagnostics

MG is a clinical diagnosis that should be suspected based upon the symptoms and findings on physical examination of variable and fatigable ptosis, diplopia, and/or ophthalmoplegia. Although MG can mimic any ophthalmoplegia presentation, the presence of combinations of ptosis or extraocular muscle weakness that do not conform to a specific pattern of ocular motor nerve paresis should prompt suspicion for MG (e.g., right ptosis and left internuclear ophthalmoplegia).

Other helpful ocular signs may be present in MG including the Cogan's lid twitch sign and enhancement of ptosis. When the patient looks down (thus resting the levator and allowing a buildup of ACh) and then looks up to primary position, the upper lid overshoots and then drifts downward or the downward drift can be followed by several twitches of the lids. Enhancement of ptosis may occur (due to Herings' law of equal innervation); by lifting the ptotic lid, the contralateral lid might fall (i.e., enhancing the ptosis). Fatigue with sustained upgaze can manifest as worsening ptosis or ophthalmologia with effort. Orbicularis oculi weakness should also be evaluated in all patients with ptosis or diplopia suspected of harboring MG (see Fig. 1).



Myasthenia Gravis, Overview, Fig. 1 Myasthenia gravis showing orbicularis oculi weakness

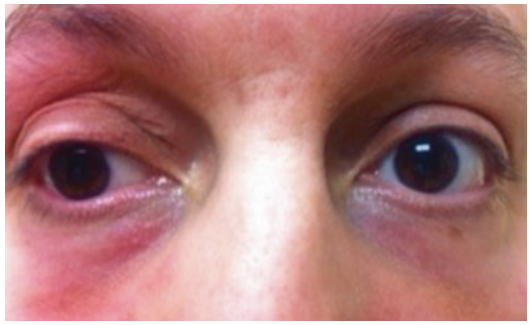


Myasthenia Gravis, Overview, Fig. 2 Myasthenia gravis ice test pre and post

Pharmacological testing in the clinic for MG includes the use of intravenous (IV) edrophonium or intramuscular (IM) neostigmine tests (both are acetylcholinesterase inhibitors). The IV edrophonium (i.e., Tensilon) test requires a good and reliable endpoint (e.g., ptosis or clearly visible ophthalmoplegia). The response to IV edrophonium is rapid (occurring within 30 s to 1 min of administration of the drug) and can be dramatic reversal of ptosis or ophthalmoplegia. The edrophonium (Tensilon) test has a sensitivity of 92% for ocular MG versus a sensitivity of 88% for generalized MG and a specificity of 97% for both ocular and generalized MG. There may be false-negative results with edrophonium testing, however, when long-standing MG is complicated by atrophy. Although rare, some complications associated with the administration of edrophonium can include diaphoresis or heart block; therefore, pre-administration of atropine is suggested and monitoring may be required in select patients. IM prostigmin can be used for longer-lasting effect and allows time to measure the ocular deviation with orthoptic examination. The side effect profile is similar to edrophonium however, and concomitant atropine administration can be used to reduce side effects. Safer and more convenient alternatives to the edrophonium test include the rest/sleep test and the ice test. The rest/sleep test consists of the patient closing his or her eyes for at least 30 min with immediate ptosis (or orthoptic) measurements after the patient opens their eyes. The ice test is another sensitive and specific test for MG. The ptosis in the ice test may show dramatic clinical improvement after ice is placed on a ptotic lid for a few minutes. The ice test is often combined with a rest test clinically. It is not clear what mechanism accounts for the ice test in MG, but some have suggested that cooling the junction prolongs the time that the Ach receptor channels are open (see Figs. 1 and 2).

Serum testing for anti-Ach receptor antibodies is useful for confirming the clinical diagnosis of MG. These antibody tests have a modest sensitivity of 44% for ocular MG, 96% for generalized MG but a higher specificity of 97–99% for MG. The ACh antibody types include binding, modulating, and blocking antibodies, and patients can be positive for one but negative for the others. The most common screening antibody obtained is the binding antibody which is detected in approximately 90% of patients with generalized MG gravis and 70% of patients with purely ocular MG. Muscle-specific tyrosine kinase (MuSK) antibodies is another serologic test that can be performed for patients with seronegative for anti-AChR antibodies. However, this test is positive in only 40% of MG patients. The antibody titer levels do not correlate with disease severity, and we order them for diagnostic purposes at initial evaluation, but we do not follow titers for prognostic or therapeutic purposes.

If the clinical suspicion remains high despite negative or inconclusive clinical and serological testing, then electrophysiological testing may be considered. Repetitive nerve stimulation (RNS), especially of the facial or proximal muscles, produces a decremental response of the muscle action potentials (more than 10% decrease) with an



Myasthenia Gravis, Overview, Fig. 3 Myasthenia gravis ice test pre and post

eventual leveling off of the amplitude. Results are more likely to be positive in patients with severe disease but may be seen in up to 40–90% of patients who have MG. Single-fiber electromyography (SFEMG) may demonstrate increased variability (jitter) in the action potentials indicating the variability of propagation time to individual fibers supplied by the same motor neuron. SFEMG is more sensitive than standard EMG for MG but is not universally available (Fig. 3).

Patients with MG should undergo imaging of the mediastinum to evaluate for the presence of a thymoma. About 10–15% of patients with MG have a thymic tumor. Hyperplasia of the thymus gland may still be present in up to age 30 years, but the persistence of the thymus gland in persons over 40 years of age is abnormal. Surgical biopsy and resection of thymoma should be performed as some of these tumors are invasive or malignant. Patients with generalized MG even without a demonstrable thymoma on chest CT scan might still benefit from thymectomy, and there are cases of complete remission after surgery. We do not recommend thymectomy without thymoma for ocular MG alone, but some benefit in select patients has also been suggested.

Differential Diagnosis

1. Chronic progressive external ophthalmoplegia
2. Oculopharyngeal muscular dystrophy
3. Myotonic dystrophy
4. Ocular motor cranial nerve palsies
5. Brainstem lesions (i.e., encephalitis, botulism, multiple sclerosis)

Prophylaxis

Several medications can cause or worsen MG (e.g., certain antibiotics, anti-arrhythmics (procainamide), ACTH and steroids, antacids with magnesium, anticonvulsants, antihypertensives (like beta-blockers or calcium channel blockers), antimalarials, anesthetic neuromuscular agents, and penicillamine), and patients should be warned about the potential side effects of these drugs on MG function.

Therapy

The main therapies for MG are supportive and conservative measures (e.g., rest, diet, avoiding medicines that worsen MG), acetylcholinesterase inhibitors (e.g., Mestinon), and immunosuppression (e.g., prednisone). We recommend symptomatic treatment of ocular abnormalities, avoidance of agents that worsen neuromuscular transmission, and thymectomy for patients with a thymoma. Pyridostigmine is an acetylcholinesterase inhibitor with a duration of action of 2–8 h. It is most useful in the treatment of systemic weakness, but less effective in the treatment of ocular MG-related ptosis or diplopia. Immunosuppressants, consisting of mainly cytotoxic agents (e.g., azathioprine, cyclophosphamide, etc.) and corticosteroids (prednisone), can be used in patients who do not respond or improve satisfactorily with acetylcholinesterase inhibitors. Prednisone may worsen MG symptoms initially, and we generally use a tapering up schedule and warn the patient about this possibility even in ocular MG patients. Plasmapheresis and IV immune globulin both produce rapid improvement in symptoms and signs, and these therapies are generally reserved for severe or potentially life-threatening MG.

Lid crutches may be used for ptosis, but in may produce severe dry eye or not be tolerated well by

patients. Lid surgery for ptosis should be reserved for patients who have stable measurements and refractory to other conservative and medical treatments. Diplopia may be managed with patching or prisms initially, but strabismus surgery may be considered in patients with stable and chronic ocular deviations who have failed a trial of conservative and medical therapy.

Prognosis

MG is a chronic disease, but some patients go into remission clinically. MG is often relapsing and remitting in course in the initial 10 years and then becomes more stable in many patients thereafter. Unfortunately, MG remains a potentially fatal disease, and patients should be warned about generalized symptoms including respiratory or swallowing difficulties that would prompt more urgent treatment and evaluation. Of MG patients presenting with ocular symptoms alone, 10–20% have spontaneous remission, while 50–70% develop generalized myasthenia gravis, usually within 2 years of onset of the disorder. In general, a younger age at onset of MG carries a better prognosis, while those who present with ocular symptoms over the age of 50 are more likely to progress to generalized MG.

Epidemiology

MG has an incidence of 1:30,000–1:20,000. The disorder has one peak occurring at 20–40 years of age, mostly in women, and another peak at 60–70 years of age, mostly in men. MG, however, may occur at any age, in any race, and in either gender even though there is an overall higher ratio of females affected than to males.

Cross-References

- ▶ Chronic Progressive External Ophthalmoplegia Plus Disease
- ▶ Demyelination, in Multiple Sclerosis, Optic Neuritis

Further Reading

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Mycobacterium chelonae Keratitis

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M

Synonyms

Atypic *Mycobacteria* keratitis; Nontuberculous *Mycobacteria* keratitis

Definition

Corneal infection caused by the atypical *Mycobacterium chelonae*. *Mycobacterium chelonae* may be difficult to differentiate in microbiological testing, and medical therapy may be challenging.

Etiology

Atypical keratitis by *Mycobacterium chelonae* is usually associated with trauma, corneal surgery, or contact lens wear. *M. chelonae* keratitis was

reported to occur after LASIK procedures in the stromal interface. *M. chelonae* is a facultative pathogenic saprophytic germ, which may cause severe opportunistic infections.

Clinical Presentation

Atypical mycobacterial keratitis is characterized by a chronic, indolent course. The characteristic presentation is a crystalline keratopathy with multiple radiating lines reminding a "cracked windshield." Mycobacterial keratitis often shows endothelial plaques, satellite lesions, and an immune ring. It may lead to nonsuppurative, indolent corneal ulcers. The post-LASIK mycobacterial keratitis may be mistaken for diffuse lamellar keratitis (DLK).

Diagnostics

Bacteriological testing is possible by direct colony growth and by a molecular test. The specimen is harvested by direct scrape from the lesion or from the smear from a LASIK flap lift.

The colony test is relatively complicated. *Mycobacterium chelonae* must be cultured on blood base agar in 2 days and 4 weeks on Lowenstein–Jensen. Subsequently, a biochemical test (i.e., nitrate reduction and niasin test) can be applied.

The suspension prepared from colonies is respectively stained with Gram staining and Ziehl–Neelsen stain (EZN) and incubated in Lowenstein–Jensen (LJ) and Mycobacterium Growth Indicator Tube (MGIT). The molecular test applies INNO-LIPA.

Differential Diagnosis

Other atypical mycobacterial keratitis
Mycotic keratitis
Nocardia species keratitis
Corynebacteria dyphteriae keratitis
Other bacterial lamellar keratitis
Diffuse lamellar keratitis (DLK)

Prophylaxis

The two main sources of the mycobacteria are air conditions in clinics and tap water. Regular check for sterility of air conditions is necessary. Tap water must be avoided in the sterilization of surgical instruments and the cleaning of contact lenses. LASIK patients should not use swimming pools up to weeks after surgery. Tap water should be avoided for the cleaning of contact lenses.

Treatment

A medical therapy as a single line is often ineffective because of delayed diagnosis, slow response to therapy, inadequate drug penetration, and resistance to most conventional antibiotics. Therefore, a surgical debridement may shorten course. In the most common case of post-LASIK infection, a flap lift and abundant irrigation is necessary and urgent.

Most authors recommend a systemic therapy with clarithromycin 500 mg twice daily combined with topical antibiotics.

The following combinations of topicals are proposed:

1. Topical Tobramycin 15 mg/mL, Azithromycin 2 mg/mL, Amikacin 25 mg/mL, and Cefazolin 50 mg/mL, every 2 h
2. Topical Clarithromycin (1%), Tobramycin (1.4%), and Ofloxacin (0.3%)
3. Tobramycin 0.3%, every 4 h plus either Gatifloxacin 0.3%, every 4 h or Moxifloxacin 0.5%, every 4 h
4. Topical Moxifloxacin 0.5% or topical ophthalmic Gatifloxacin 0.3%

The duration to treatment is 2 months for systemic antibiotics and at least 4 months for topical medication.

The use of topical Fluoroquinolone monotherapy without concomitant systemic Clarithromycin should be avoided to prevent the forming of resistant strains. Ophthalmic steroids should be avoided.

Prognosis

The visual outcome of patients with ***Mycobacterium chelonae*** **keratitis** varies, depending on the location of the infiltrates relative to the visual axis and the size and the severity of the infiltrates. Patients may develop scars with loss of corneal transparency and irregular hyperopic astigmatism. Penetrating keratoplasty may be necessary in some cases.

Epidemiology

Mycobacterium chelonae keratitis can be epidemic if surgical instruments are the source of the infection.

Cross-References

- ▶ Endophthalmitis
- ▶ Keratitis
- ▶ Lamellar Keratoplasty

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Mydriasis Induced Secondary Angle Closure

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Definition

Angle closure is defined by iridotrabecular contact (either reversible apposition of the peripheral iris to the trabecular meshwork or irreversible *peripheral anterior synechiae* (*PAS*)), followed by reduced outflow of aqueous humor through the anterior chamber angle. In susceptible individuals, angle closure may occur due to mydriasis, which can be induced by various factors.

Etiology

Mydriasis induced angle closure is provoked by obstruction of aqueous flow both at the level of the iris and the pupil.

Resistance to transpupillary aqueous flow increases physiologically on dilation, with a maximum at mid-dilated pupil position. Additionally, in susceptible individuals (usually in patients with a narrow or occludable anterior chamber angle), a thick peripheral iris may "roll" into the trabecular meshwork and result in angle closure with subsequent elevation of intraocular pressure (IOP).

Mydriasis can be induced by various factors including not only dilating drops but also systemic drugs with sympathomimetic or parasympatholytic activity, as well as activation of sympathetic system by pain or emotional upset.

Typical systemic drugs with potential for precipitating angle closure in susceptible individuals are nebulized bronchodilators, selective serotonin re-uptake inhibitors, allergy and cold medications, tricyclic antidepressants, muscle relaxants, and some urological drugs.

Clinical Presentation

Angle closure secondary to mydriasis may present as *acute angle closure* with ocular pain and headache, red eye, mild dilated and nonreactive pupil, iris bombé, photophobia, decreased or blurred vision, and halos.

Mydriasis induced angle closure may also present intermittent, with recurrent episodes of blurred vision, halos and mild pain, often beginning in the evening in dark rooms, or during situations of stress with activation of the sympathetic system, and resolving spontaneously, often during sleep, and can therefore be misinterpreted as headache or migraine.

On clinical examination, there may be signs of previous angle closure attacks.

Intermittent angle closure may also progress to chronic angle closure with mild to moderate elevation of IOP and glaucomatous optic neuropathy (GON).

Typically, mydriasis induced angle closure occurs in eyes with a symmetric narrow anterior chamber angle.

Diagnosis

Angle closure is diagnosed on *gonioscopy.* Dynamic gonioscopy helps to distinguish between appositional angle closure and PAS.

Gonioscopy reveals a narrow anterior chamber angle in both eyes.

In chronic angle closure, dynamic gonioscopy may reveal PAS in patients with modest elevation of IOP and GON.

Ultrasound of the anterior segment may reveal additional structural changes of the peripheral iris.

Tonometry reveals elevated IOP.

Biomicroscopy with accurate assessment of the anterior chamber as well as the posterior segment is mandatory in classifying angle closure. Previous ocular and medical history, family history, as well as subjective symptoms should be inquired to exclude or confirm previous attacks in case of acute or intermittent angle closure.

Visual field examination, *retinal nerve fiber layer* assessment, and optic disc imaging should be performed to assess the stage of disease.

Provocative tests with simultaneous miotic therapy and dilator muscle stimulation by phenylephrine (Mapstone provocative test) in patients with narrow angle provide little information, since even when negative they may not rule out the potential for angle closure. In addition, they may trigger an acute angle closure even while the patient is monitored.

Differential Diagnosis

Primary angle closure due to pupillary block should be considered as well as any secondary angle closure with elevated IOP, either neovascular glaucoma, *uveitic glaucoma*, *lens-induced angle closure*, and angle closure due to aqueous misdirection (*malignant glaucoma*) or to choroidal pathologies (e.g., *uveal effusion*).

Also consider any *secondary open angle glaucoma* with acute rise of IOP like inflammatory, *corticosteroid glaucoma*, *Posner-Schlossmann-Syndrome*, *pseudoexfoliative glaucoma*, *pigmentary glaucoma*, *ghost cell glaucoma*, *phacolytic glaucoma*, or open angle glaucoma due to intraocular malignant tumors.

Prophylaxis

Dapiprazole is an alpha-receptor blocker that reverses pharmacological pupil dilation. Although it may not eliminate the possibility of angle closure, it reduces the overall time of dilation and especially the critical period of mid-dilated pupil in patients with narrow angle.

In patients with narrow angle on gonioscopy, a prophylactic iridotomy may be considered (*angle closure suspect*).

Therapy

Treatment of mydriasis induced glaucoma depends on the clinical presentation and stage of disease.

Medical treatment includes topical hypotensive medication like *beta-blocker*, *alpha agonists*, and *prostaglandin analogues*, topical steroids to

prevent PAS formation, and systemic aqueous humor suppressants, either *carbonic anhydrase inhibitors* or hyperosmotic agents.

Mild topical *miotic agents* may be effective by pulling the peripheral iris away from the anterior chamber angle, but they may also have an adverse effect by increasing the iris-lens contact and in consequence a pupillary block mechanism.

Indentation of the cornea may open the anterior chamber angle by shifting the fluid in the anterior chamber into the periphery.

The definitive treatment is iridectomy, either laser or surgical. In some cases, *peripheral laser iridoplasty* may be necessary prior to iridotomy to flatten the peripheral iris.

Prognosis

Only a small percentage of individuals with a narrow angle develop *acute angle closure* on mydriasis. No valid tests exist to predict which patients are at risk.

Epidemiology

Female gender, older age, and hyperopia are factors associated with shallower anterior chambers and may predispose for angle closure secondary to mydriasis, although estimates of risk vary greatly.

Cross-References

- ▶ Acute Angle Closure
- ▶ Angle Closure
- ▶ Angle-Closure Glaucoma
- ▶ Altitudinal Visual Field Defects
- ▶ Ghost Cell Glaucoma
- ▶ Iridotomy
- ▶ Lens-Induced Angle-Closure Glaucoma
- ▶ Malignant Glaucoma
- ▶ Pigmentary Glaucoma
- ▶ Posner-Schlossman Syndrome
- ▶ Pseudoexfoliative Glaucoma
- ▶ Secondary Angle-Closure Glaucoma
- ▶ Secondary Open-Angle Glaucoma
- ▶ Ultrasound
- ▶ Uveitic Glaucoma

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Myopic Chorioretinal Atrophy and Lacquer Cracks

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Introduction

Chorioretinal atrophy corresponds to the dry myopic maculopathy. While its features have been described many years ago, there is no widely accepted definition of the condition and its different stages.

In the present section, tessellated fundus, diffuse and patchy atrophy, and lacquer cracks will be considered as part of the myopic chorioretinal atrophy syndrome.

Epidemiology, Physiopathology

Epidemiological studies consistently show high myopia as the third or the fourth cause of legal blindness in developed countries, with a higher prevalence of affected patients in Asia than in western countries. However, these studies usually mix dry and wet subtypes of myopic maculopathy, i.e., nonneovascular and neovascular cases. Fundus analysis of patients with high myopia (refractive error – 6 dp or higher) showed that three fourth of myopic eyes present with myopic maculopathy with most cases presenting the dry forms: lacquer cracks, tessellated fundus, patchy or diffuse chorioretinal atrophy, and macular

atrophy (3%). Myopic dry maculopathy is usually bilateral (Soubrane and Coscas 2001; Silva 2012; Ohno-Matsui 2014).

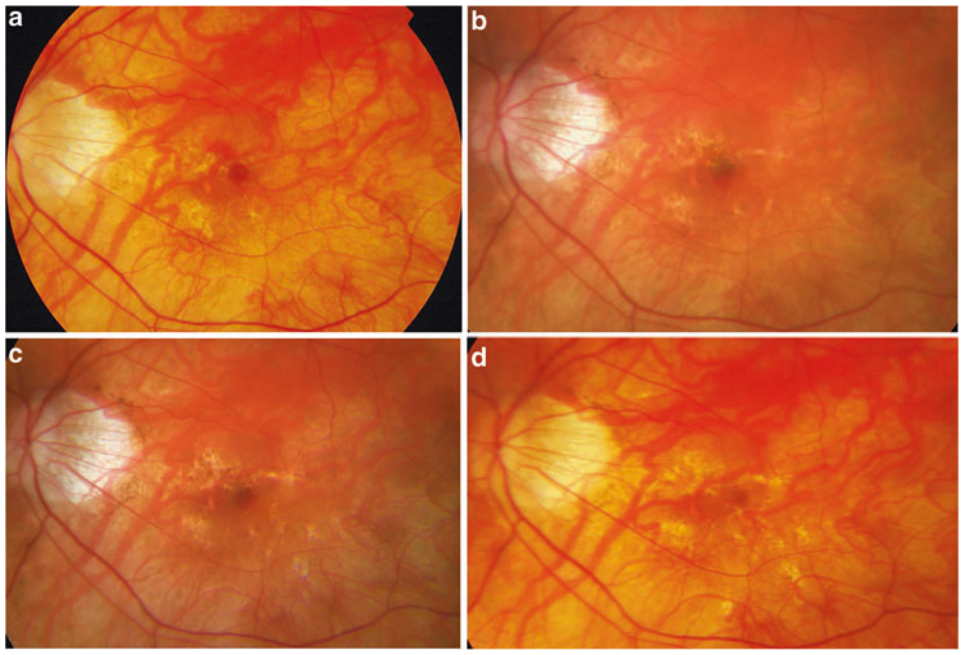
Myopic chorioretinal atrophy is considered as the consequence of the progressive elongation of the eyeball, resulting in a progressive thinning of the retinal pigment epithelium and the choroid. Elongation of the Bruch's membrane may lead to mechanical fissures, resulting in lacquer cracks. Rarefaction of the choroid, with a relative sparring of the retinal pigment epithelium, may account for the occurrence of diffuse chorioretinal atrophy, while disappearances of RPE and choriocapillaris are distinctive features of patchy areas of chorioretinal atrophy.

Progressive elongation of the eyeball explains the progression of the myopic maculopathy with age. Tessellated fundus may be observed in young myopic individuals, but the other stages are more frequently observed later in age. Myopic choroidal neovascularization may complicate the course of the disease at any stage of the myopic maculopathy.

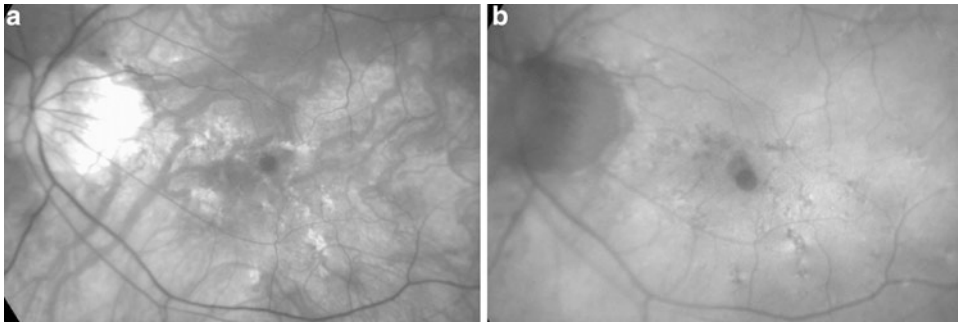
Clinical Description

Tessellated fundus is the consequence of axial elongation which causes a relative hypoplasia of the RPE, allowing an increased visibility of the choroidal vessels (Fig. 1a). Tessellation frequently occurs initially around the optic disk and could extend slowly during life in different directions according to the axis of the staphyloma. In eyes with tessellated fundus, fluorescein angiography shows a decreased contrast of the fundus during dry transit due to a higher reflection of the sclera. This poor contrast may also explain the difficulty of localization of the foveal avascular zone. Optical coherence tomography usually shows a relatively thin retina and choroid.

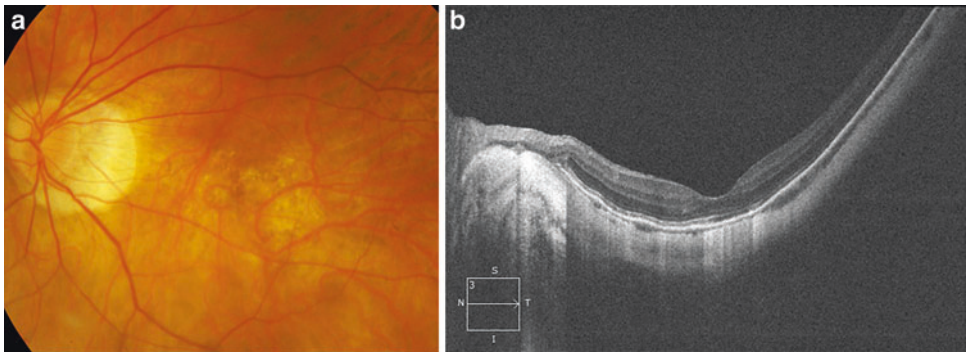
Eyes with tessellated fundus may be relatively stable, without progression toward more severe stages. Visual acuity may be strictly normal, despite reduced amplitude and delayed latency observed in multifocal ERG.



Myopic Chorioretinal Atrophy and Lacquer Cracks, Fig. 1 (**a**) Tessellated fundus with pallor of the fundus and abnormal visibility of the choroidal vessels. (**b**–**d**) Occurrence and extension of lacquer cracks, observed as multiple, horizontally oriented, branching, and crisscrossing *white lines*



Myopic Chorioretinal Atrophy and Lacquer Cracks, Fig. 2 (a) Red-free picture and (b) autofluorescence picture of a myopic female, showing the lacquer cracks as white in red-free light and dark in autofluorescence



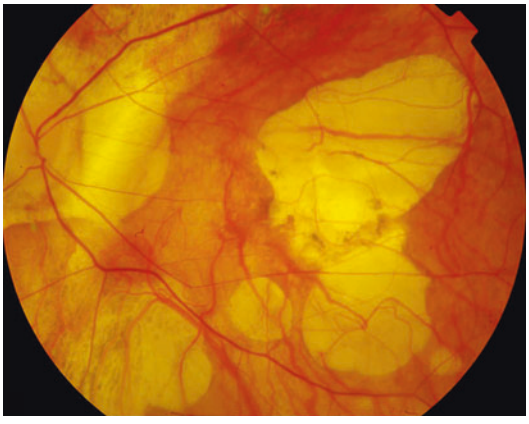
Myopic Chorioretinal Atrophy and Lacquer Cracks, Fig. 3 (**a**, **b**) Color and red-free picture of a myopic fundus showing diffuse myopic atrophy with yellowish appearance of the fundus, more obvious in the area located between the disk and the fovea. (**c**) Horizontal scan of the OCT showed that the choroid is very thin, but that there is no thinning of the retina

M

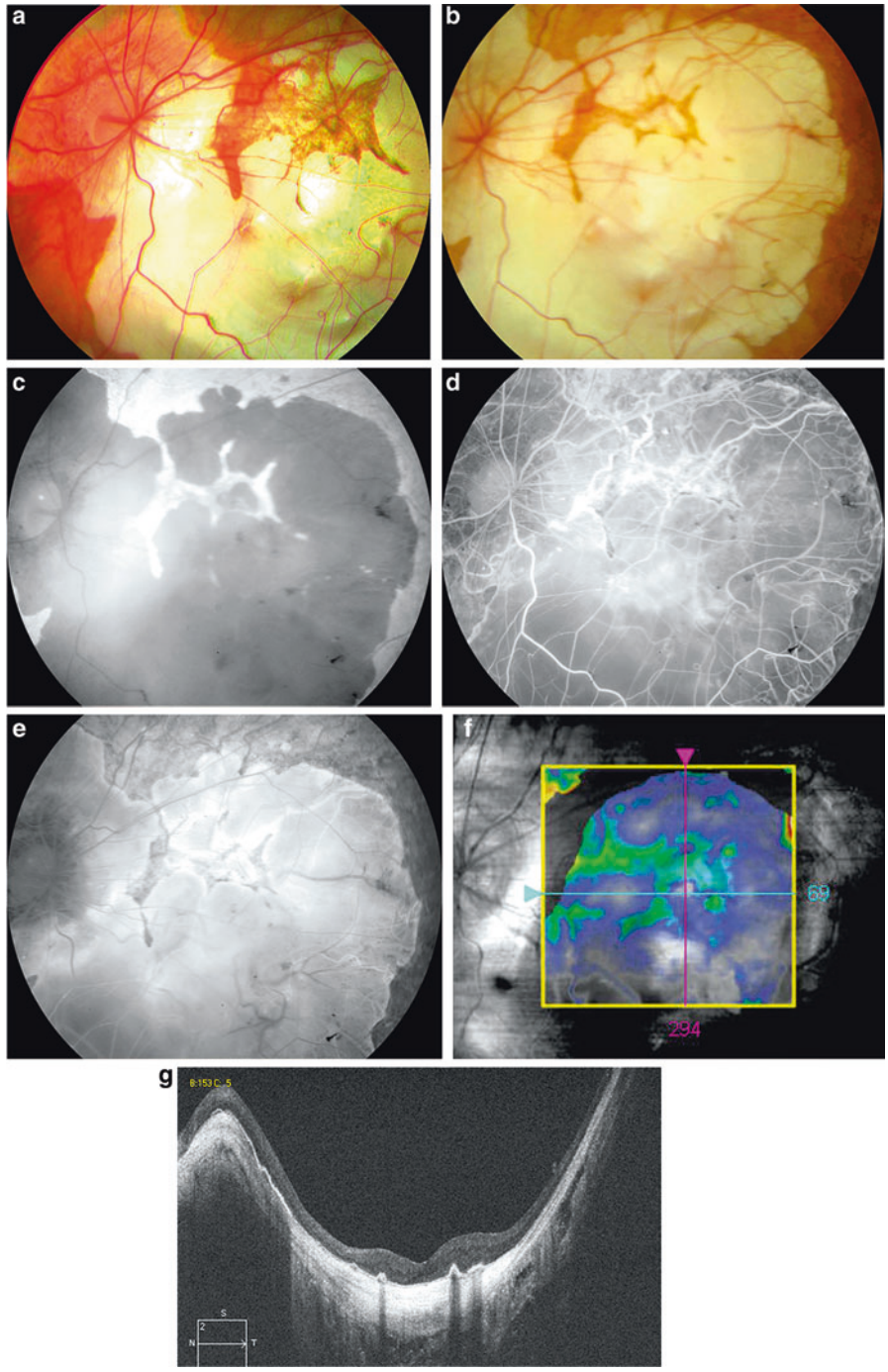
Lacquer Cracks

Lacquer cracks correspond to fine, irregular in caliber, yellowish or white, single and frequently horizontally oriented, or multiple and often branching and crisscrossing lines of the fundus. They are located in the posterior pole in the area of the staphyloma. They are rarely observed in the young age, and their frequency distribution could be with two peaks of age, one before 40 and one after 55.

Occurrence of lacquer cracks is usually associated with subretinal hemorrhages, usually small and regressive (Fig. 1b, c). Visual acuity loss or paracentral scotoma may be the revealing symptoms of the condition, according to the location of the bleeding. Usually, hemorrhages are fine and homogeneous, different from the ones that are



Myopic Chorioretinal Atrophy and Lacquer Cracks, Fig. 4 Patchy chorioretinal atrophy. Large areas of atrophy with lightly pigmented margins



Myopic Chorioretinal Atrophy and Lacquer Cracks, Fig. 5 Patchy chorioretinal atrophy. (**a**, **b**) Color photographs showing the extension of large areas of chorioretinal areas. (**c**) Autofluorescence: the atrophic areas are dark. (**d**, **e**) Fluorescein angiography showing absence of choriocapillaris, increased visibility of choroidal vessels, and progressive staining of the sclera. (**f**, **g**) OCT: irregular thinning of the retinal mapping. Horizontal scan showed that the choroid is almost absent

associated with choroidal neovascularization. Lacquer cracks may be observed after resorption of the hemorrhages. Lacquer cracks are hypo-autofluorescent (Fig. 2). Fluorescein angiography shows the cracks as lines that are hyperfluorescent during the entire sequence. ICGA shows the lines as hypofluorescent during the entire sequence. OCT may miss the lacquer cracks because lesions are narrow. However, attentive examination with multiple scans usually shows the cracks as discontinuities of the RPE and Bruch's membrane with deep hyper-reflectivity due to the deep penetrance of the light signal.

It is frequent that patients with one lacquer cracks develop additional lesions with time (Fig. 1a–d). Lacquer cracks also enlarge with time. Their impact on visual acuity is usually minimal. However, enlargement of subfoveal cracks and/or consequences of subfoveal bleeding may lead to irreversible visual loss.

Diffuse Chorioretinal Atrophy

Diffuse chorioretinal atrophy corresponds to a yellowish appearance of the fundus. Lesions are ill defined and sometimes difficult to observe (Fig. 3a). They typically occur around the optic nerve and slowly extend in the area of the staphyloma. They occur in the midlife and their frequency increases with age and with axial length. They are asymptomatic, and VA is preserved in most cases. Autofluorescence is usually normal. FA may show a tiny late hyperfluorescence of the fundus. In ICGA, eyes usually present a rarefaction of choroidal vessels. OCT may be more informative, showing a marked thinning of the choroid, without thinning of the retina (Fig. 3b).

Focal Chorioretinal Atrophy

Focal or patchy chorioretinal atrophy corresponds do the development of small areas of depigmentation. Patchy atrophy is more frequent with age and in eyes with long axial length. Its prevalence could exceed 50% in eyes with axial length superior to 32 mm. Lesions typically are white or yellowish and correspond to the visualization of the sclera through transparent retina. Large choroidal vessels may be seen in these areas. The margins of these patchy atrophic lesions may be pigmented (Fig. 4). The lesions are hypo-autofluorescent due to lack of RPE. OCT shows the absence of RPE and attenuation of the choroid. Fluorescein angiography shows the choroidal vessels, without the usual hyperfluorescence of the choriocapillaris (Fig. 5). Thus, areas of atrophy are hypofluorescent in the early stages of FA and show slow and progressive hyperfluorescence due to staining of the dye at the scleral level. Course of patchy atrophy is characterized by extension and coalescence of atrophic areas. It could also be complicated by myopic foveoschisis which typically occurs and extends in these areas. Despite extension of patchy atrophy, involvement of the fovea is relatively rare. Thus, visual acuity remains good in most eyes with patchy chorioretinal atrophy.

Conclusion

Dry myopic maculopathy is a common finding in myopic eyes. Most lesions occur and develop with age and elongation of axial length. Visual acuity is preserved in most cases, except when patchy atrophy of central lacquer cracks extends in the subfoveal area. Multimodal imaging of the lesions, including autofluorescence and spectral-domain OCT, helps to better characterize the lesion in order to evaluate the visual prognosis.

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N

NA-AION

► Nonarteritic Anterior Ischemic Optic Neuropathy

N-Acetylgalactosamine-4-Sulfatase Deficiency

► Maroteaux-Lamy Syndrome

Nail-Patella Syndrome

► Onychoosteodysplasia (Nail-Patella Syndrome)

NAION

► Nonarteritic Anterior Ischemic Optic Neuropathy

Nanophthalmos

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Synonyms

Microphthalmia; Microphthalmos

Definition

An ocular length <20.5 mm with mostly normal function. It is associated with hyperopia and a very shallow anterior chamber (Fried et al. 1982). Since nanophthalmic eyes have a crystalline lens of normal size, there is a high risk of glaucoma due to angular or cilio-lenticular block from the second or third decade of life. The sclera and choroid is often thickened, and serous ablation may occur. Nanophthalmic eyes are at high risk for surgical complications such as cilio-lenticular block and choroidal effusion (Brockhurst 1974).

A congenital nanophthalmos can occur separately or in conjunction with syndromes. Both sporadic occurrence and familiar associations have been described.

Histology

A significantly thickened sclera, with less ordered collagen bundles, and a thickened choroid are typical findings. Immunohistochemistry showed increased levels of fibronectin and proteoglycans in the sclera of nanophthalmic eyes for fibronectin (Yue et al. 1988). Other changes (retinal atrophy, macular edema) can be found as secondary changes.

Molecular Diagnostics

Recently, defects on chromosome 11 have been reported (Othman et al. 1998; Sundin et al. 2005).

U. Schmidt-Erfurth, T. Kohnen (eds.), *Encyclopedia of Ophthalmology*,
https://doi.org/10.1007/978-3-540-69000-9

In the presence of other anomalies, a syndrome has to be considered. There are numerous reports of rare syndromes associated with nanophthalmos. Therefore, the decision for special molecular diagnostics has to be made individually.

Differential Diagnosis

Microphthalmia secondary to other conditions such as persistent primary hyperplastic vitreous, ROP-associated retrolental fibroplasia, and phthisis bulbi.

Cross-References

- ▶ Angle-Closure Glaucoma
- ▶ Malignant Glaucoma
- ▶ Microphthalmos (Microphthalmia)

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Narrow Angle

▶ Angle-Closure Suspect

Narrow Angle Glaucoma

▶ Primary Angle Closure and Angle Closure Glaucoma

Narrow Drainage Angle

▶ Primary Angle Closure and Angle Closure Glaucoma

Narrow-Angle Glaucoma

▶ Angle-Closure Glaucoma

Nasoethmoid Orbital Fractures

▶ Naso-Orbital-Ethmoid Fractures

Naso-Orbital-Ethmoid Fractures

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Synonyms

Nasoethmoid orbital fractures; Naso-orbito-ethmoid fractures; NOE fractures

Definition

The naso-orbital-ethmoid (NOE) region is the region lateral to the nasal bones and medial to the medial canthus. NOE fractures involve the lower 2/3 of the medial orbital rim, where the medial canthal tendon inserts. The classic NOE fracture pattern involves fractures of the lateral nose, the inferior orbital rim, the medial orbital ethmoid wall, the nasal maxillary buttress at the pyriform aperture, and the junction of the frontal

process of the maxilla with the internal angular process of the frontal bone. Though this is the classic fracture pattern, significant variation exists (Cummings 2005). Markowitz classified NOE fractures into three types based on the relationship of the medial canthal tendon to the fracture lines and resulting bone fragments. NOE fractures may be unilateral or bilateral (Figs. 1, 2, 3, 4, and 5).

Basic Characteristics

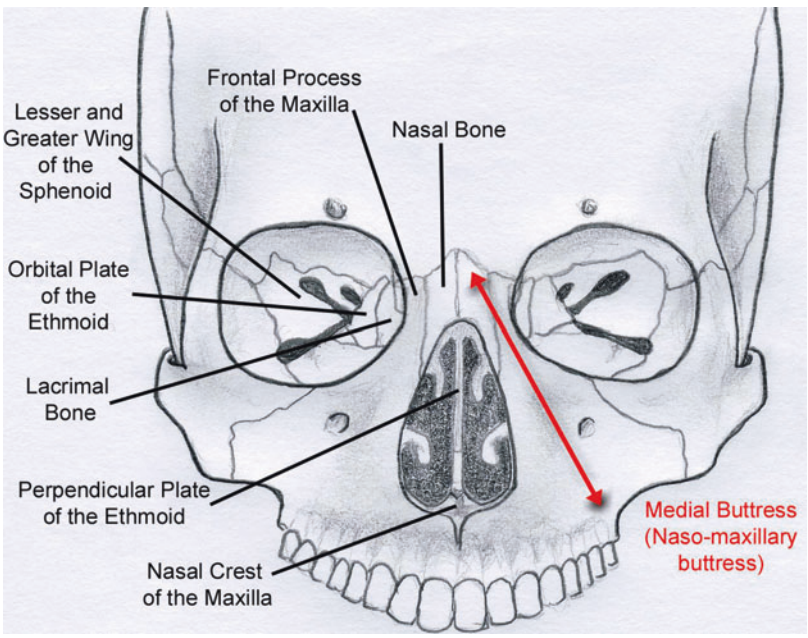
Etiology

NOE fractures are generally the result of blunt-force trauma to the midface. Common causes include motor vehicle accidents, interpersonal altercations, assaults, falls, and sports-related injuries.

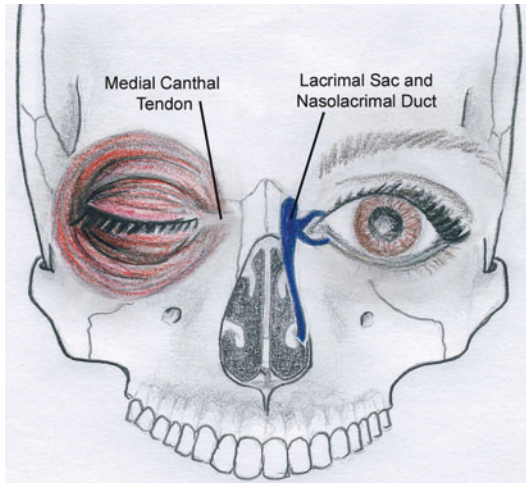
Clinical Presentation

Facial fractures often occur as the result of significant trauma and evaluation should begin with airway control and hemodynamic stabilization. Spinal cord injury should be ruled out, and any overt globe injury should be evaluated. A thorough history and physical, including a complete head and neck exam, may then be performed. With any midfacial fracture, suspicion for CSF rhinorrhea and/or otorrhea should be high.

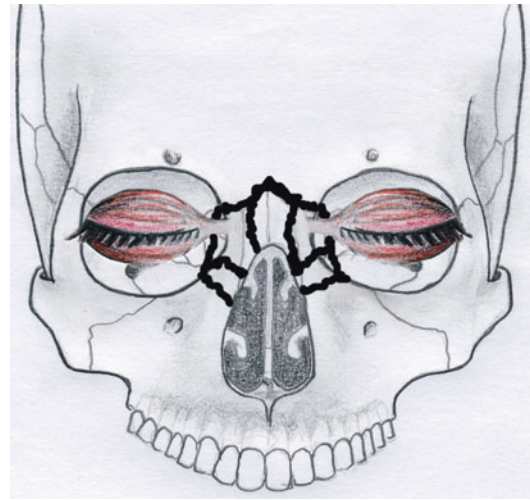
The NOE area plays a key role in midfacial contour and nasal projection and has important relationships to surrounding soft tissue structures that influence the clinical signs of a NOE fracture (Stewart 2005). Patients with NOE fractures may present with a short and sunken nasal bridge. Step-offs may be palpable along the nasal dorsum or medial orbital rim. Crepitus may often be felt over the medial canthus. The medial canthal tendon splits to envelop the lacrimal sac and attaches to the anterior and posterior lacrimal crests, frontal process of the maxilla, and internal angular process of the frontal bone and plays a key role in supporting the globe and eyelid. When the medial canthal tendon attachment is disrupted, the medial canthus retracts laterally leading to an increased intercanthal distance and shortening of the palpebral fissure; an intercanthal distance of greater than 35 mm is suggestive of NOE fracture and a distance of greater than 40 mm is virtually diagnostic (Marcowitz et al. 1991). The lacrimal system may be disrupted by NOE fractures and injury to the lacrimal canaliculi can result in epiphora. The trochlea is located on the internal angular



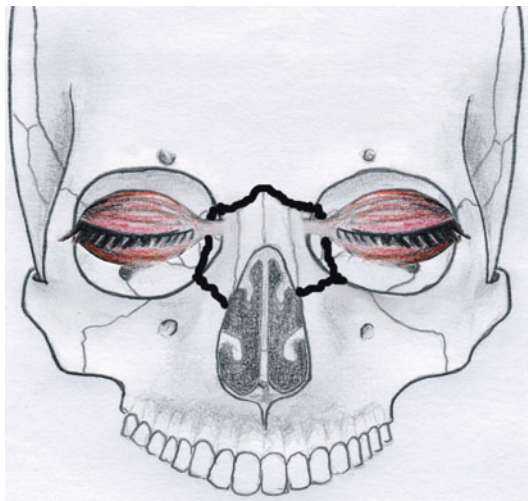
Naso-Orbital-Ethmoid Fractures, Fig. 1 Bony anatomy of the naso-orbital-ethmoid region



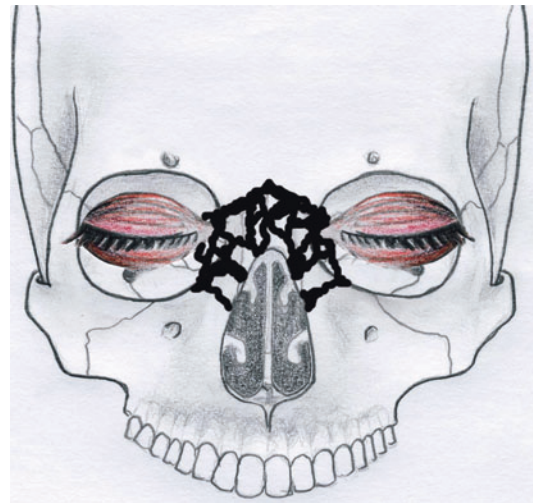
Naso-Orbital-Ethmoid Fractures, Fig. 2 Relationship of the naso-orbital-ethmoid complex to the medial canthal tendon and lacrimal apparatus



Naso-Orbital-Ethmoid Fractures, Fig. 4 Markowitz Type II naso-orbital-ethmoid fractures result in multiple bone fragments, though the fractures do not extend into the area of the attachment of the medial canthal tendon



Naso-Orbital-Ethmoid Fractures, Fig. 3 Markowitz Type I naso-orbital-ethmoid fractures result in a single bone fragment into which the medial canthal tendon inserts



Naso-Orbital-Ethmoid Fractures, Fig. 5 Markowitz Type III naso-orbital-ethmoid fractures result in numerous bone fragments, and importantly, the fracture lines extend through the bone into which the medial canthal tendon inserts, disrupting the medial canthal tendon. In this case, canthal avulsion may be present

process of the frontal bone and injury may cause extraocular muscle disturbance and diplopia. Patients may present with severe epistaxis either from Keisselback's plexus anteriorly, or branches of the sphenopalatine, or anterior ethmoid arteries posteriorly. Bleeding from the ethmoid vessels can also cause periorbital ecchymosis. Significant facial edema is common, and it is important to keep in mind that presence of a NOE fracture does not rule out presence of additional maxillofacial injuries.

Diagnostics

NOE fractures involve orbital wall fractures, and a complete ophthalmic exam is necessary. Intracranial injury must also be ruled out, and suspicion for CSF rhinorrhea should be high. CT scan is considered the modality of choice for diagnosis of NOE fractures (Papel 2002).

Treatment

Treatment of ocular and CNS injuries should precede treatment of NOE fracture in the presence of a stable airway. In patients with multiple facial fractures, most authors advocate repair of associated facial fractures prior to repair of NOE fractures. Reduction of maxillary and frontal fractures can restore important landmarks that are used to guide repair of the NOE fracture. A combination of incisions may be required to gain adequate exposure. Commonly employed incisions include bicoronal, lynch, inferior orbital rim, subciliary, transconjunctival, and sublabial. When possible, existing lacerations should be used to gain access. Repair of NOE fractures should reposition the displaced bony fragments with reattachment of the medial canthal tendon if needed. Perioperative antibiotics should be strongly considered in patients with facial fractures.

Cross-References

- ▶ Blowout Fractures
- ▶ Guerin (Maxillary) Fracture
- ▶ Le Fort Fractures
- ▶ Orbital Floor Fracture
- ▶ Orbit, Inflammation of
- ▶ Zygomatic Bone
- ▶ Zygomatic-Maxillary Complex Fractures

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Naso-Orbito-Ethmoid Fractures

▶ Naso-Orbital-Ethmoid Fractures

Nd:YAG Laser

▶ Nd:YSGG Laser, for Intrastromal Photodisruption

Nd:Yag-Capsulotomy

▶ Capsulotomy

Nd:YSGG Laser, for Intrastromal Photodisruption

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Synonyms

Nd:YAG laser

Definition

Epithelial ingrowth into the space between the corneal cap and stromal bed may occur in up to 3% of myopic LASIK surgeries (Yanoff and Duker 2013). If left untreated, ingrowth can lead to inflammation mimicking keratitis, irregular astigmatism, and loss of BCVA (Azar 2007). The traditional method for removing epithelial

ingrowth was a surgical flap lift to remove the cells underneath it. This exposed stroma may be treated with alcohol solution to limit epithelial cell regrowth again. The flaw is that the practice of re-lifting the flap results in a high rate of recurrence of epithelial ingrowth (Linfield et al. 2012). The use of laser technology (e.g., Nd:YAG laser), however, has shown promise in eliminating further epithelial ingrowth.

Indication

Early intervention with laser treatment (Nd:YAG laser) for removal of epithelial ingrowth following LASIK is recommended to eliminate further flap lift and epithelial ingrowth (Linfield et al. 2012).

Contraindication

Laser procedure using Nd:YAG is contraindicated if there are corneal scars, irregularity, or edema. Further contraindications include: poor eye stability, known or suspected cystoid macular edema, and possible active inflammation of the eye.

Techniques and Principles

The neodymium:yttrium-aluminum-garnet (Nd:YAG) laser is a laser with a wavelength of 1,064 nm. The Nd:YAG laser causes optical breakdown with a short, high-power pulse (Lindfield and Poole 2013). Focusing the laser upon the epithelial ingrowth creates a localized plasma-mediated vacuole, evaporating surrounding tissue.

The eye is initially prepared with topical anesthesia, and then the Nd:YAG laser is focused on the corneal epithelium (Lindfield and Poole 2013). The energy level for the laser ranges from 0.2 to 0.6 mJ. The beam is then defocused to reach the region of epithelial ingrowth. It is recommended that, if apparent, the laser be targeted at the septum that bridges the island of cells and the flap edge to block migration. The treatment begins at the center of this area of epithelial ingrowth and is gradually enlarged to the periphery. A gap should be kept between the tissue bubbles to avoid overlap of targeted areas.

Outcome

Patients report improved vision, resolution of subjective visual complaints and symptoms of glare, and possible diplopia (Linfield et al. 2012). The therapeutic benefits of Nd:YAG laser treatment for epithelial ingrowth has not been fully investigated. Additional studies are necessary to compare Nd:YAG laser versus mechanical treatment of epithelial ingrowth.

Complications

No adverse effects have been reported to date for this laser treatment of epithelial ingrowth (Linfield and Poole 2013). As with any procedure, risk remains for potential further epithelial ingrowth, infection, increased intraocular pressure, retinal detachment, macular edema, hemorrhage, corneal edema, and corneal endothelial loss.

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Near-IR Digital Photography

► Infrared Digital Photography

Necrotizing Fasciitis, of Orbit

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Definition

Necrotizing fasciitis is a bacterial infection that spreads through the subcutaneous tissue planes and results in destruction of the fascia and fat but may spare the skin. It is characterized by symptoms such as edema, crepitus, blisters, subcutaneous gas, and disproportionate pain. It is also distinguished by marked systemic symptoms, such as shock and organ failure, which can lead to death. Necrotizing fasciitis often involves the extremities, abdominal wall, and perineum but may rarely involve the head, neck, and periorbital region (Anaya and Dellinger 2007; Sarani et al. 2009).

Etiology

Two clinical types of necrotizing fasciitis exist. Type 1 infections are polymicrobial and are caused by a mixture of aerobic and anaerobic bacteria, such as *Staphylococcus aureus*, enterobacteriaceae (e.g., *E. coli*, *Pseudomonas* species, and *Klebsiella* species), enterococci, and streptococci. This type usually occurs after surgical procedures or in patients with diabetes and peripheral vascular disease. Type 2 infections are caused by group A streptococcus (GAS), such as *Streptococcus pyogenes. Staphylococcus aureus* and its methicillin resistant form have also been implicated in type 2 necrotizing fasciitis (Wong et al. 2003; Sarani et al. 2009).

Epidemiology

Necrotizing fasciitis has an annual incidence of about 1,000 cases per year in the United States or about 0.04 cases per 1,000 person-years. It has a cumulative mortality rate of about 24–34%. One review found that 10% of necrotizing fasciitis cases involved the head and neck. However, it rarely affects the eyelid due to its rich vascular supply. Only 58 cases of well-documented eyelid necrotizing fasciitis have been reported over 50 years (Wong et al. 2003; Anaya and Dellinger 2007; Sarani et al. 2009).

Risk Factors

Risk factors for developing necrotizing fasciitis include (Wong et al. 2003):

Alcoholism
Diabetes mellitus
Systemic malignancy
Systemic corticosteroid use
Rheumatologic disease
Minor blunt traumas, lacerations, or previous surgery

Clinical Presentation

Early recognition of necrotizing fasciitis is important because the disease can progress rapidly into a systemic illness with significant morbidity and mortality. Necrotizing fasciitis can present with signs and symptoms of cellulitis, including erythema and edema of the affected area. Key features to look for are pain out of proportion to the skin findings, signs of systemic toxicity, and blister or bullae formation. Occasionally, severe pain without any cutaneous findings is the only manifestation of the infection (Wong et al. 2003; Elner et al. 2006).

Within 1–2 days of the initial presentation, erythema can develop or darken into a cyanotic color. Blisters and bullae filled with serous fluid often develop soon afterwards and should raise the suspicion of necrotizing fasciitis. By this stage, extensive deep tissue destruction has already occurred and patients usually present with fever and signs of systemic toxicity.

Necrotizing fasciitis of the eyelid, however, may have a different clinical course compared to

other areas of the body due to its rich blood supply and lack of subcutaneous tissue between the orbital septum and the orbicularis oculi muscle (Lukisch et al. 2002). The rich blood supply spares the eyelid margins from necrosis and allows systemic antibiotics to have better access to infected areas. The close proximity between the skin, orbital septum, and orbicularis oculi muscle also allows the infection to be noticeable earlier in the course of the disease. This allows rapid initiation of treatment. In addition, the orbicularis oculi muscle may serve as a barrier against spread of the infection into the periorbit. Necrotizing fasciitis may involve both eyes because of minimal resistance to spread of infection in the subcutaneous tissue over the nose (Elner et al. 2006).

Diagnostics

The history and clinical findings usually point to the diagnosis of necrotizing fasciitis. It should be considered when patients present with fever, systemic toxicity, and pain out of proportion to the skin findings. One retrospective study devised criteria for diagnosing necrotizing fasciitis based on six common laboratory tests (Wong et al. 2004). Each of the tests has assigned points, and the total score has a range of 0–13. A total score of $\geq$6 raises the suspicion for the infection with a 50–75% chance of developing the disease. A score of $\geq$8 has a >75% chance of accurate diagnosis. The lab values with their scores are as follows:

Serum C-reactive protein $\geq$ 150 mg/L (4 points)
Total white blood cell count 15,000–25,000/μL (1 point) or > 25,000/μL (2 points)
Hemoglobin 11.0–13.5 g/dL (1 point) or $\leq$ 11 g/dL (2 points)
Serum sodium < 135 mEq/L (2 points)
Serum creatinine > 1.6 mg/dL (2 points)
Serum glucose > 180 mg/dL (1 point)

Elevated serum lactate and creatinine kinase can also be seen in necrotizing fasciitis.

In addition, imaging studies can be done to help with the diagnosis, especially in cases of uncertainty. Plain radiography and a CT scan can be done to assess for air or gas along the facial planes. CT scans can also assess for deep tissue infection, particularly deep abscesses. CT and MRI with or without enhancement have also been used to show increased thickness of the facial layer, which can be associated with necrotizing fasciitis. However, obtaining an MRI may be prohibited in clinically unstable patients and can result in inappropriate delays in treatment. An emergent non-contrast CT scan offers a more expeditious option.

Differential Diagnosis

Cellulitis
Abscess
Gas gangrene (clostridial myonecrosis)
Pyomyositis
Myositis (viral/parasitic)

Treatment

Treatment of necrotizing fasciitis includes the use of systemic broad-spectrum antimicrobial therapy, such as β-lactam antibiotics (e.g., penicillin), cephalosporins, and clindamycin. Clindamycin may be more effective than penicillin because it inhibits both toxin production and streptococcal M protein synthesis, an antiphagocytic virulence factor that prevents leukocytic attack. However, clindamycin should be used in combination because rare cases of GAS strains resistant to clindamycin have been observed. In cases suspected of having type 1 disease, clindamycin can be used to provide anaerobic coverage. Other therapeutic options include monotherapy with a beta-lactam-beta-lactamase inhibitor (e.g., pipercillin-tazobactam) or a carbapenem (Anaya and Dellinger 2007; Sarani et al. 2009).

In most cases of necrotizing fasciitis, prompt surgical treatment is important in decreasing mortality. However, the unique anatomy of the eyelid with its rich vascular supply and thin skin allows for conservative treatment with delayed debridement (Lukisch et al. 2002). The vasculature of the eyelid enables

systemic antibiotics to have better access to infected areas and gives the zone of tissue adjacent to necrotic tissue better local blood supply. One study recommended conservative management by observing patients until a clear zone of demarcation is apparent at which time bedside debridement of the necrotic skin can be done. This allows for a significantly less amount of tissue to be removed than the amount that would be excised if aggressive debridement to the edge of the advancing infection were done. However, aggressive debridement is important in severe cases in which infection extends into the orbit and beyond the periorbital area (Elner et al. 2006).

Hyperbaric oxygen has also been evaluated as an adjunctive treatment for necrotizing fasciitis. It may decrease mortality and limit the amount of debridement needed by inhibiting toxin production. However, results from studies are conflicting, and no epidemiology-based studies have been done to show the effect of hyperbaric oxygen on necrotizing fasciitis.

Prognosis

The mortality rate of patients with periorbital spread of necrotizing fasciitis that involves the scalp and upper face is about 12.5%. No deaths have been reported that are solely due to necrotizing fasciitis of the eyelids, but significant morbidity often ensues. The low likelihood of mortality from eyelid infections is presumably due to the eyelid's unique anatomic features. As mentioned previously, the skin of the eyelid is thin, and the lack of subcutaneous fat between the skin and the orbicularis oculi muscle allows necrosis of the eyelid to occur rapidly, making the presence of the infection known. It is thus less likely to spread or be contained in the eyelid for prolonged periods where it could potentially act as a nidus for further infection.

However, cases of deep orbital involvement by spread of the infection along the orbital septum and blood vessels have been reported. In these cases, arterial occlusion due to severe perivascular involvement leading to thrombosis can occur and lead to blindness secondary to retinal arterial occlusion. Further ischemic necrosis can also occur due to increased intraorbital pressure from severe inflammation and edema. Early surgical intervention and medical therapy can prevent visual loss in these cases.

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Necrotizing Keratitis

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Synonyms

Corneal necrosis; Necrotizing stromal keratitis

Definition

Necrotizing stromal keratitis is a condition characterized by the presence of severe inflammation in the corneal tissue and subsequent damage leading to destruction of the corneal tissue, necrosis, and corneal melting seen in response

to an inflammatory or infectious process. In the more severe forms, the condition can progress to corneal abscess formation (a condition that is referred as suppurative keratitis), thinning, and perforation.

Etiology

A variety of pathologic processes could present as necrotizing keratitis. The major etiologies can be classified into one of these categories:

1. Infectious: a wide spectrum of infectious agents including bacterial, viral, fungal, and protozoal infections of the cornea could be associated with corneal ulceration and necrotizing keratitis. (For a more detailed and in-depth information about each of these entities, the reader is referred to the related section elsewhere in this encyclopedia.)

   A special form of necrotizing keratitis associated with an infectious etiology is necrotizing herpetic keratitis. Intact virions have been detected in stromal keratocytes and lamellae on electron microscopic examination of pathologic tissue from patients with herpetic necrotizing stromal keratitis. The use of topical corticosteroids without antiviral coverage has been implicated as a possible risk factor (Krachmer and Mannis 2010).
2. Immune mediated: a variety of systemic immune-mediated diseases and vasculitic diseases like rheumatoid arthritis (RA), relapsing polychondritis, and Wegener's granulomatosis can be associated with corneal melting and peripheral ulcerative keratitis (PUK). Corneal involvement in these conditions is more commonly associated with an adjacent scleritis, but it can occur as isolated finding. (For a more detailed and in-depth information about each of these entities, the reader is referred to the related section elsewhere in this encyclopedia.)
3. Toxic reaction to certain drugs: corneal melting could be a drug-related complication in conditions like anesthetic abuse or the use of the alkylating agent mitomycin C as an antifibrotic agent in pterygium and glaucoma filtering (Krachmer and Mannis 2010). The topical use of NSAIDs like diclofenac, ketorolac, and bromfenac has also been associated with the risk of corneal melting. However a definitive link between topical NSAIDs and corneal melts has not been documented (Kim et al. 2010). Alkylating agents like mitomycin C are also associated with corneal melting (Copeland and Afshari 2013).

In addition, corneal melting and necrosis may be the final consequence of a prolonged and persistent epithelial defect due to a variety of etiologies including chemical burn, exposure keratopathy, and ocular surface disease like keratoconjunctivitis sicca, Stevens-Johnson syndrome, and graft versus host disease.

In these conditions, the cornea may be the primary site affected by the pathologic process, with or without secondary involvement of adjacent structures like the sclera or anterior chamber in its course, or, sometimes, the cornea may be secondary affected by extension of adjacent pathology like necrotizing scleritis.

Clinical Presentation

Due to the diversity of the etiology of necrotizing keratitis, the clinical presentation may take different forms based on the etiology of the disease.

The symptoms in patients with an infectious keratitis commonly include variable degrees of pain, ocular discomfort, photophobia, blepharospasm, tearing and eye injection, and blurred vision. The onset of symptoms may take an acute and fulminant form (hours to a few days) in cases with virulent bacterial organisms like *Pseudomonas aeruginosa* or a more protected and prolonged course (several days to weeks) in less virulent organisms like fungal, nocardial, and mycobacterial infections.

The clinical findings in these patients include adnexal reaction with erythema and eyelid swelling; conjunctival injection and eyelid edema; ciliary flush dense stromal infiltration with opacification, necrosis, and abscess formation; and ulceration and which may be accompanied

with an overlying epithelial defect. Other signs may include anterior chamber reaction and hypopyon formation. (For more information regarding the specific characteristics of each type of keratitis, the reader is referred to the related sections elsewhere in this encyclopedia.)

The clinical findings in necrotizing herpetic stromal keratitis are corneal necrosis, ulceration, and dense infiltration of the stroma with an overlying epithelial defect. The combination of replicating virus and severe host inflammatory response may progress to corneal thinning and perforation in a short period of time. The clinical findings in this condition may resemble those of infectious keratitis secondary to other infectious keratitides. Therefore, bacterial and fungal pathogens must be ruled out when this diagnosis is considered.

Keratitis in rheumatologic disease like RA occurs most often contiguous with adjacent area of scleritis, but it may occur as an isolated finding. The clinical picture may take different like sclerosing keratitis, acute stromal keratitis, limbal guttering, peripheral ulcerative keratitis, and keratolysis (Krachmer and Mannis 2010).

Diagnosis

The workup for patients with necrotizing keratitis should be tailored for each patient according to the clinical setting to address the possible causative etiologies.

A detailed history with particular attention to drug history, previous surgeries, and ocular and other symptoms suggestive of an underlying ocular disease like herpes simplex and systemic disease is crucial.

A full ophthalmic examination with particular attention to the lids, lid margin, conjunctiva, cornea, and other anterior segment and posterior segment structures is necessary to define the full extent and stage of the disease.

If an infectious etiology is suspected, corneal scraping and obtaining smear and culture with appropriate stain and media are indicated to identify the causative organism. Corneal biopsy and molecular diagnostic tests like polymerase chain reaction (PCR) may be helpful in some patients. (For a more detailed discussion, refer to section "Infectious Keratitis".)

Although herpetic keratitis is most commonly diagnosed clinically, identification of organism with viral culture, antigen detection methods, or PCR can be used to confirm the diagnosis in selected cases (Knickelbein et al. 2009). In patients with an immune-mediated corneal melting, a meticulous workup to rule out an underlying systemic disease is essential, not only to control the eye disease, but the ophthalmologist may play a life-saving role, considering the high mortality rate associated with untreated systemic disease. In patients suspected to have an underlying systemic disease, a systemic examination and adjunctive laboratory tests may be necessary to identify the underlying disease. A battery of tests commonly used includes CBC with diff, urinalysis, chest X-ray, erythrocyte sedimentation rate or C-reactive protein, rheumatoid factor (RF), antinuclear antibody (ANA), and antineutrophil cytoplasmic antibodies (ANCA). However, the workup needs to be individualized based on each clinical setting (Copeland and Afshari 2013).

Differential Diagnosis

- Infectious keratitis due to bacterial, viral, fungal, and protozoal infestations of the cornea
- Immune-mediated corneal disease in the context of systemic autoimmune disease (as previously addressed in the etiology) or local immune-mediated disease like Mooren ulcer and Fuchs marginal keratitis
- Toxic effects related to anesthetic abuse, certain drugs like topical NSAIDs
- Corneal and sclera melts associated with surgeries like pterygium excision particularly with adjunctive use of mitomycin C

Prophylaxis

The Herpetic Eye Disease Study (HEDS) showed the beneficial effects of prophylaxis with oral acyclovir (400 mg BID) in reducing the

recurrence rate in patients with a history of previous epithelial and stromal keratitis. Although the study recommendations do not distinguish between different types of stromal keratitis and the results may not be directly applicable to herpetic necrotizing keratitis considering that this condition probably represents the least common type of herpetic keratitis, the same recommendations probably should be undertaken in herpetic necrotizing keratitis in the view of the pathogenesis of this condition (Knickelbein et al. 2009).

Therapy

The management of a patient presenting with necrotizing keratitis should be individualized based on the possible etiology, severity of the disease, and the presence of other concomitant ocular or systemic diseases and requires a careful implantation of available medical and surgical measures targeted to address the causative etiology and other interventions that may be necessary to save the tectonic structural integrity of the eye. Sometimes, a multidisciplinary approach and consultation with other subspecialities may be required in recalcitrant cases of peripheral ulcerative keratitis associated with other systemic diseases.

If an offending agent or drug could be identified as the trigger for the insult, discontinuation of the exposure could be a very important step in preventing further progression of the disease.

In patients with necrotizing keratitis with an infectious etiology, control of infection with appropriate topical antibiotics in conjugation with systemic antibiotics in selected cases is essential. This generally requires an aggressive and intensive treatment with fortified antibiotic drops, effective against the causative organism. Progressive corneal melting and small perforations may be amenable to tissue adhesives like cyanoacrylate glue. Large perforations and threatened scleral involvement may need therapeutic keratoplasty in an emergent setting to control the infection. Amniotic membrane transplantation has been reported in infectious keratitis patients and may be helpful in some cases. Collagen cross-linking is also being investigated in the treatment of infectious keratitis. (For a more detailed discussion, refer to the section "Infectious Keratitis".)

Necrotizing herpetic stromal keratitis is especially difficult to manage and may rapidly progress to corneal perforation. Necrotizing herpetic keratitis patients are treated with a combination of antivirals and corticosteroids. Due to toxicity of topical antivirals, systemic antivirals are preferred in patients with necrotizing HSV stromal keratitis. Transplantation of amniotic membrane onto the ocular surface that promotes healing of the corneal epithelium and reduces stromal inflammation has been used with promising results in the management of necrotizing HSV stromal keratitis.

Prognosis

Prognosis depends on the underlying disease.

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Necrotizing Scleritis

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Synonyms

Necrotizing scleritis with inflammation

Definition

An aggressive form of scleritis that is an inflammatory disease of the sclera often accompanied by severe pain and risk of vision loss

Etiology

Necrotizing scleritis is caused by antigen-antibody complex deposition in the vessels as part of type II hypersensitivity reaction (Goldstein and Tessler 2009; Biber et al. 2011). There is inflammation of macrophages, B cells, and T cells. Most of the T cells are of the CD4 T helper cell type (Biber et al. 2011). In 50–81% of cases, there is an underlying vasculitic disease (Biber et al. 2011). Necrotizing scleritis may also be induced from surgery or after the use of bisphosphonates or mitomycin (Sharma and Rosenbaum 2010). The necrotizing form of scleritis comprises 75% of surgically induced scleritis (Biber et al. 2011). This can occur after any procedure and can include cataract surgery, penetrating keratoplasty, strabismus surgery, or pterygium excision (Biber et al. 2011).

Clinical Presentation

Patients often present with severe pain and discomfort that wakes them up from sleep. This gradual onset pain may radiate to the brow or jaw (Kanski and Bowling 2011). On examination, there is congestion of the deep vascular plexus of the anterior eye, often with a purplish/blue hue from underlying uvea. These vessels do not blanch with topical phenylephrine, and red-free light may help determine the anatomical level of inflammation (Goldstein and Tessler 2009). There are also areas of white, avascular sclera. Necrotizing scleritis is bilateral in 60% of patients, but may also be unilateral or move from eye to eye (Goldstein and Tessler 2009; Kanski and Bowling 2011). Perforation often does not occur, but can occur in cases of elevated IOP or ocular trauma.

Necrotizing scleritis has three categories: vasoocclusive, granulomatous, and surgically induced. The vasoocclusive form shows patches of scleral edema that may coalesce (Kanski and Bowling 2011). Vasoocclusive necrotizing scleritis is most often associated with rheumatoid arthritis (Kanski and Bowling 2011). The granulomatous form presents with raised, irregular, and edematous sclera and overlying tissue (Kanski and Bowling 2011). The granulomatous form is often associated with Wegener granulomatosis (Kanski and Bowling 2011). Finally, the surgically induced form may present within 3 weeks of procedure up to many months later.

Diagnosis

Lab diagnosis is not specific for scleritis, but may help determine the underlying systemic disease. An incomplete list but important lab tests include rheumatoid factor (RF), antineutrophil cytoplasmic antibody (ANCA), antiphospholipid antibodies, antinuclear antibodies (ANA), complete blood count (CBC), erythrocyte sedimentation rate (ESR), and urinalysis (Biber et al. 2011; Kanski and Bowling 2011).

Differential Diagnosis

Episcleritis

- Mild instead of severe pain
- Fiery, brick red appearance instead of blue/purple color
- Avascular areas absent
- No necrosis or scleral thinning

Conjunctivitis

- Discharge present
- Superficial inflammation blanches with phenylephrine

Anterior uveitis

Prophylaxis

Unclear

Therapy

Oral NSAIDs work well for non-necrotizing scleritis, but in necrotizing scleritis, systemic corticosteroids are indicated. Prednisone is often used. There may also be a need for systemic immunosuppressive drugs in severe cases, and cyclophosphamide is often used in those with Wegener's granulomatosis (Biber et al. 2011). Treatment with immunosuppressive drugs is recommended until scleritis is controlled for 1 year (Biber et al. 2011). These immunosuppressives are often needed for long-term treatment of scleritis after the use of prednisone for 3–6 months (Goldstein and Tessler 2009). TNF-α biologic therapies are less studied but have been used clinically.

Surgical therapy is rarely needed. In cases with emergent perforations, a tectonic scleral and peripheral corneal patch grafting should be used.

Prognosis

Even when treated, necrotizing scleritis carries the greatest risk for vision loss of any type of scleritis. Eighty-two percent of necrotizing scleritis patients lost visual acuity (Biber et al. 2011). Other complications that may present include sclerosing keratitis, peripheral ulcerative keratitis, uveitis, glaucoma, or perforation (Sharma and Rosenbaum 2010; Biber et al. 2011; Kanski and Bowling 2011). Uveitis occurs in one-third of necrotizing scleritis patients (Biber et al. 2011). Cataract may also develop, but cataract treatment is postponed until the scleritis is in remission for at least 2–3 months (Goldstein and Tessler 2009; Sharma and Rosenbaum 2010). If the scleritis is treated and the scleritis resolves, the sclera will heal. Necrotizing scleritis also carries a risk of mortality with an 8-year mortality of 21% (Goldstein and Tessler 2009).

Epidemiology

The average age of onset for necrotizing scleritis is 60 (Kanski and Bowling 2011). It occurs in all races. Many cases have an underlying systemic disorder, which is most often a connective tissue disease. Underlying disease can include psoriatic arthritics, inflammatory bowel disease, rheumatoid arthritis, relapsing polychondritis, Wegener's granulomatosis, and polyarteritis nodosa (Goldstein and Tessler 2009; Biber et al. 2011).

Cross-References

- ▶ Conjunctivitis
- ▶ Episcleritis: Overview

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Necrotizing Scleritis with Inflammation

▶ Necrotizing Scleritis

Necrotizing Scleritis Without Inflammation

▶ Scleromalacia: Overview

Necrotizing Stromal Keratitis

▶ Necrotizing Keratitis

Necrotizing Viral Retinitis

▶ Acute Retinal Necrosis (Necrotizing Herpetic Retinitis)

Neodymium:YAG Laser

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Definition

The neodymium-yttrium-aluminum-garnet (Nd:YAG) laser is an example of a pulsed laser concentrating low amounts of energy into very brief periods (Atebara and Thall 2004).

Clinical Features

Besides Nd:YAG laser capsulotomy, the peripheral iridotomies are routine treatments. The frequency-doubled Nd:YAG laser (532 nm green) can be used for photocoagulation treatments.

Treatment

The 1064 nm infrared Nd:YAG laser works on the principle of photodisruption which is mainly a mechanical effect. Highly focused laser pulses induce an optical breakdown. Vapor formed by the lightning bolt expands, quickly collapses, and produces a miniature thunder clap. Acoustic shock waves cause most of the tissue damage (Atebara and Thall 2004). Nd:YAG lasers do often work in the Q-switching mode: a shutter in the laser cavity blocks laser light emission until a large population inversion has been established. The shutter is opened quickly, and the burst lasts about one millionth of a second (Atebara and Thall 2004). Since the infrared light is invisible, a helium-neon laser is implemented causing a red aiming beam. Due to different light bending properties, the focus of the Nd:YAG laser rarely coincides precisely with the aiming beam (Atebara and Thall 2004).

Cross-References

▶ Angle-Closure Glaucoma
▶ Capsular Bag Opacification

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Neovascular Glaucoma in Diabetes Mellitus

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Synonyms

Neovascular glaucoma in proliferative diabetic retinopathy

Definition

Neovascular glaucoma is a blinding disease, difficult to manage and often resulting in disastrous visual loss (Allingham et al. 2005). In 1906, Coats described new vessel formation on the iris in eyes with central retinal vein occlusion. Thus increased intraocular pressure with iris neovascularization and/or angle neovascularization appearing in patients with proliferative diabetic retinopathy (PDR) with and without retinal detachment and with or without any previous intraocular surgery is defined as neovascular glaucoma in diabetes mellitus.

Etiology

Diabetic retinopathy is the most common cause of rubeosis iridis accounting for approximately one third of patients with neovascular glaucoma. Neovascular glaucoma is an advanced manifestation of diabetic retinopathy. Neovascular glaucoma may occur without retinal or optic disk neovascularization; however, it is more commonly seen in association with PDR. The frequency with which rubeosis iridis is associated with diabetic retinopathy is greatly influenced by surgical interventions. After pars plana vitrectomy for diabetic retinopathy, the reported incidence ranges from 10% to 42%, whereas that for neovascular glaucoma ranges from 10% to 23%, with most of the cases developing during the first 6 months after surgery (Hayreh 2007). In these cases, the occurrence of rubeosis iridis and neovascular glaucoma is much higher in aphakic eyes (as compared to phakic or pseudophakic) and when rubeosis is present before the vitrectomy. An unrepaired retinal detachment after vitrectomy for diabetic retinopathy is also a risk factor for postoperative rubeosis iridis. A completely attached retina and aggressive anterior or peripheral photocoagulation therapy have been shown to be the most important factor in controlling or preventing neovascular glaucoma after vitrectomy for PDR. Intraocular silicone oil also reduces the incidence of anterior segment neovascularization, possibly acting as a diffusion or convection barrier. Hypoxia of the retina in areas of capillary nonperfusion causes neovascularization via angiogenic substances, mainly vascular endothelial growth factor (VEGF) produced by Müller cells.

Clinical Presentation

The prevalence of rubeosis iridis among patients with diabetes mellitus ranges from 0.25% to 20% according to various reports. Diabetes usually exists for many years before rubeosis develops, and concomitant PDR is usually found. In patients with PDR, approximately 50% of cases have rubeosis iridis. If rubeosis iridis is seen in a patient with nonproliferative diabetic retinopathy, other causes such as carotid artery disease should be considered. The risk of rubeosis iridis and neovascular glaucoma in patients with diabetic retinopathy greatly increases when arteriolar or capillary nonperfusion is present or after vitrectomy or lensectomy. In looking for the earliest biomicroscopic evidence of anterior segment rubeosis, it is important to pay close attention to the pupillary margin of the iris, where neovascularization is typically seen first. However, gonioscopy is also important, because angle neovascularization may occasionally precede that of the iris.

Diagnostics

In diabetic retinopathy, fluorescein angiography of the retina to confirm (or exclude) proliferations at the optic nerve head or elsewhere is crucial. A careful biomicroscopic examination or indirect ophthalmoscopy should be performed to rule out peripheral retinal detachment. For detection of rubeosis iridis, careful slit-lamp examination and in doubt fluorescein angiography of the iris may help to differentiate dilated iris capillaries from neovascularization. Measuring of intraocular pressure and careful gonioscopy to differentiate between open-angle and angle-closure stage of neovascular glaucoma is mandatory.

Differential Diagnosis

All other causes predisposing to rubeosis iridis and neovascular glaucoma should be considered. They include all retinal ischemic diseases such as ischemic central or hemicentral retinal vein occlusion (CRVO), retinal detachment, hemorrhagic retinal disorders, Coats exudative retinopathy, Eales disease, Leber's congenital amaurosis, retinopathy of prematurity, persistent hyperplastic primary vitreous, sickle cell retinopathy, syphilitic retinal vasculitis, retinoschisis, Stickler syndrome, and optic nerve glioma with subsequent venous stasis retinopathy. Other causes such as irradiation retinopathy, intraocular tumors or lymphoma, and inflammatory diseases or surgically induced rubeosis and extraocular causes such as

carotid artery obstruction or occlusion and fistula should also be considered to cause rubeosis iridis.

Prophylaxis

Panretinal photocoagulation is most effective as prophylaxis against the development of neovascular glaucoma. The mechanism by which panretinal photocoagulation influences neovascularization is uncertain, although it may be related to decreasing the retinal oxygen demand. This hypothesis is consistent with the reported observation that the photoreceptor-retinal pigment epithelial complex accounts for two thirds of the retinal oxygen consumption. Decreased oxygen demand may reduce the stimulus for release of an angiogenesis factor or may reduce the hypoxia in the anterior ocular segment. Panretinal photocoagulation is mandatory in diabetic patients undergoing pars plana vitrectomy for PDR and should be performed during the vitrectomy using endophotocoagulation. Cataract surgery in patients with PDR should be delayed until panretinal photocoagulation has been performed.

Therapy

The first-line treatment is lowering of the IOP with topical or systemic medications, which may indirectly improve retinal perfusion. Suppression of angiogenesis by repeated intravitreal injection of anti-VEGF substances (ranibizumab, bevacizumab, or aflibercept) has been recently shown to significantly decrease anterior segment neovascularization (Beutel et al. 2010; SooHoo et al. 2015). In addition to anti-VEGF, intravitreal injections of steroids (triamcinolone) may reduce the inflammatory stimulus but may increase the IOP especially in steroid responders. Reducing the oxygen demand of the retina by laser coagulation of the ischemic retina significantly reduces or eliminates anterior segment neovascularization. If medical IOP lowering is not effective enough, surgery (trabeculectomy or tube shunts) may be required. Surgically lowering IOP by trabeculectomy has been shown to be very effective in lowering the rate of recurrence of anterior segment neovascularization. When cloudy media precludes panretinal photocoagulation, transscleral panretinal cryotherapy, often combined with cyclocryotherapy, can control the IOP and reduce the neovascularization.

Prognosis

If neovascular glaucoma is diagnosed early enough (before the chamber angle is completely closed), aggressive photocoagulation may reverse the anterior segment rubeosis and the increased IOP in a majority of cases. With modern vitrectomy techniques using endophotocoagulation and when indicated silicone oil, the percentage of postsurgical neovascular glaucoma has been significantly reduced. Maintaining the posterior capsule in cataract surgery has also reduced the risk of postsurgical rubeosis in diabetic patients.

Epidemiology

No exact data are available about the prevalence of neovascular glaucoma in patients with PDR. There is, however, some data on increased mortality rates and reduced life expectancy in patients requiring tube shunt implants for neovascular glaucoma (Blanc et al. 2004).

Cross-References

▶ Neovascular Glaucoma in Ischemic Central Retinal Vein Occlusion

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Neovascular Glaucoma in Ischemic Central Retinal Vein Occlusion

► Neovascular Glaucoma in VOR

Neovascular Glaucoma in Ocular Ischemia, Others

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Definition

Ocular ischemic syndrome is a serious but uncommon blinding condition. Increased intraocular pressure with iris neovascularization and/or angle neovascularization appearing in patients with carotid artery obstruction is defined as neovascular glaucoma (NVG) in ocular ischemia (Allingham et al. 2005). Neovascular glaucoma may also be present in other extraocular vascular disorders such as internal carotid occlusion or carotid-cavernous fistula and in a variety of intraocular disorders such as retinal detachment, hemorrhagic retinal disorders, Coats exudative retinopathy, Eales disease, Leber's congenital amaurosis, retinopathy of prematurity, persistent hyperplastic primary vitreous, sickle cell retinopathy, syphilitic retinal vasculitis, retinoschisis, Stickler syndrome, and optic nerve glioma with subsequent venous stasis retinopathy. Other causes such as irradiation retinopathy, intraocular tumors or lymphoma, and inflammatory diseases or surgically induced rubeosis may also responsible for NVG.

Etiology

Carotid artery obstructive disease is probably the third most common cause of neovascular glaucoma (after proliferative diabetic retinopathy and ischemic central retinal vein occlusion), accounting for 13% of all cases. Neovascularization is caused by reduction of global blood flow to the eyeball, which can produce anterior and/or posterior segment ischemia. Anterior segment ischemia results in development of iris and angle neovascularization and NVG. Most patients with ocular ischemic syndrome have severe carotid artery occlusive disease, but not all; it can be associated with vascular occlusive disease of the aortic arch or of the ophthalmic, central retinal or ciliary arteries. In contrast to the other causes of NVG, not only retinal but also uveal ischemia may be an important contributing factor for neovascularization.

NVG may also be diagnosed following radiation for a variety of ocular and orbital lesions, e.g., iris melanoma, posterior uveal melanomas, choroidal metastatic tumors, retinoblastoma, orbital lymphoma, and nasal and paranasal malignancies. In ocular radiation, in most eyes the main factor responsible for the development of NVG most likely is the development of secondary radiation retinopathy, in which there is development of retinal capillary non-perfusion and retinal ischemia. NVG has been reported, prior to treatment, in ring melanoma of the anterior uvea, adenocarcinoma of the nonpigmented ciliary epithelium, medulloepithelioma, circumscribed choroidal hemangioma, metastatic cutaneous melanoma to the vitreous, retinoblastoma, and metastatic malignant lymphoma. Development of NVG has been observed following anterior as well as posterior uveitis, with or without underlying systemic disease. NVG may also develop in miscellaneous retinal diseases as retinal vasculitis per se or when it is associated with systemic diseases, such as Crohn's disease and Behcet's disease. Other

miscellaneous retinal conditions which may be associated with development of NVG include Coats disease, Eales disease, frosted branch angiitis, giant cell astrocytoma of the retina, peripheral retinal detachment, and X-linked retinoschisis. Similarly other systemic diseases, e.g., cryoglobulinemia and Churg-Strauss syndrome, by causing retinal vascular occlusion, can be associated with (NVG Löffler 2006).

Clinical Presentation

Eyes with neovascularization due to ocular ischemia may initially be normotensive or even hypotensive due to decreased perfusion of the ciliary body with reduced aqueous production, and fluorescein angiography may reveal an increased arm-to-retina time and leakage from the retinal arterioles. Previous to neovascularization, patients may have had one or several episodes of amaurosis fugax, especially if the stenosis of the carotid is more than 50%. The anterior chamber in these eyes often shows the presence of flare. Sometimes a few cells may be seen as well. As in the other forms of NVG, rubeosis iridis starts at the pupillary margin of the iris but may be also present already in the chamber angle (Oderich and Lawrence 2002). Posterior synechia may be seen, and if there is extensive synechia formation, patients may present with acute angle-closure glaucoma due to pupillary seclusion. In a majority of patients there are some lens opacities. However, in a fully developed NVG with very high IOP, the clinical picture may be dramatically different; the eye may be painful, and, when the IOP goes very high fairly fast, there is usually corneal epithelial edema which can make examination for iris and angle neovascularization difficult.

Diagnostics

For detection of rubeosis iridis, careful slit-lamp examination and in doubt fluorescein angiography of the iris may help to differentiate dilated iris capillaries from neovascularization. Measuring of intraocular pressure and careful gonioscopy to differentiate between open-angle and angle-closure stage of neovascular glaucoma is mandatory. A careful biomicroscopic examination or indirect ophthalmoscopy should be performed to find the cause of retinal hypoxia and to rule out peripheral retinal detachment or intraocular tumors. Fluorescein angiography should be performed to measure arm-to-retina time and to exclude other causes of anterior segment neovascularization especially proliferative diabetic retinopathy and ischemic central retinal vein occlusion.

In cases of suspected ocular ischemic syndrome due to carotid artery obstruction, it is not uncommon in clinical practice to find that carotid artery disease is ruled out as the cause of ocular ischemia based on the findings of absence of occlusion or severe stenosis of the internal carotid artery on carotid Doppler. However, carotid Doppler evaluates only the artery in the neck and not above or below that, where it may be markedly stenosed. Cerebral angiography or magnetic resonance angiography may be necessary to provide information which carotid Doppler cannot demonstrate, such as significant stenosis in the carotid siphon or ophthalmic artery (Hayreh 2007).

Differential Diagnosis

From time to time, NVG has been confused with other ocular conditions. For example, eyes with severe non-granulomatous uveitis with dilated iris vessels and proteinous aqueous and high IOP can be misdiagnosed to have NVG. There are some eyes where normal iris vessels are seen easily, particularly in blue eyes, which may be mistaken for iris neovascularization or even angle neovascularization when the vessels are seen near the root of the iris. Eyes with carotid-cavernous fistula erroneously may be diagnosed to have NVG because of the blood in Schlemm's canal and the elevated IOP.

Prophylaxis

There is no primary prophylaxis for NVG in ocular ischemic syndrome. A high index of suspicion

of its development is important for early diagnosis and treatment to prevent irreversible visual loss. Ocular ischemic syndrome may be overlooked or misdiagnosed, primarily because of its diverse and sometimes subtle presentation. Ocular ischemic syndrome can also masquerade as several other ocular conditions. In patients who develop NVG from any cause, it is important to avoid development of nocturnal arterial hypotension, to prevent visual loss.

Therapy

Management of ocular ischemic syndrome remains difficult and controversial. As the main cause for neovascularization is uveal vascular insufficiency, the conventional use of panretinal photocoagulation will not control the disease. Moreover, rise of IOP following panretinal photocoagualtion may further compromise the already highly precarious ocular and optic nerve head circulation and result in severe visual loss due to development of anterior ischemic optic neuropathy or retinal ischemia. Since internal carotid artery occlusive disease is the most common cause of ocular ischemic syndrome, carotid endarterectomy seems a logical management. However, the benefit of carotid endarterectomy in patients with ocular ischemic syndrome is unknown and controversial, especially patients with initially good visual acuity may profit. Clinical decision for carotid endarterectomy is usually driven by the patient's entire clinical picture, as determined by neurologists and the vascular surgeon. Since, in ocular ischemic syndrome, perfusion pressure in the various ocular vascular beds is low, lowering IOP to as low level as possible is crucial to improve the blood flow and thereby to prevent visual loss from various types of ocular vascular occlusion (including central retinal artery occlusion and anterior ischemic optic neuropathy) and/or glaucoma.

Eyes with uveitis and retinal vasculitis are at risk of developing NVG. Thus, their appropriate management is important to prevent development of NVG. The treatment depends upon cause of these inflammatory diseases. In most of the eyes with uveitis, topical steroids and mydriatics are primary management tools; however, some patients with uveitis require systemic corticosteroids or other immunosuppressive therapies. Since most of these patients have an associated systemic disease, management of that is also essential.

Prognosis

If neovascular glaucoma is diagnosed early enough (in the stage of rubeosis iridis or open-angle glaucoma stage), aggressive treatment of the underlying cause (i.e., carotid endarterectomy in carotid occlusive disease) may reverse anterior segment neovascularization or even NVG (Shazly and Latina 2009). Once the angle is closed, prognosis is very poor despite all conventional and surgical IOP-lowering treatments. In this stage, the majority of eyes may go blind because of absolute glaucoma or phthisis bulbi.

Epidemiology

Neovascular glaucoma is a rare form of glaucoma, accounting for less than 5% of glaucoma cases. Because of its bad prognosis, NVG is one of the most frequent diagnoses (16–42%) among eyes that have to be enucleated.

Cross-References

- ▶ Neovascular Glaucoma in Ischemic Central Retinal Vein Occlusion
- ▶ Neovascular Glaucoma in Proliferative Diabetic Retinopathy

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Neovascular Glaucoma in Proliferative Diabetic Retinopathy

► Neovascular Glaucoma in Diabetes Mellitus

Neovascular Glaucoma in VOR

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Synonyms

Neovascular glaucoma in ischemic central retinal vein occlusion

Definition

In 1906, Coats described new vessel formation on the iris in eyes with central retinal vein occlusion. Rubeosis iridis is frequently associated with a severe form of glaucoma, which may best described with the term neovascular glaucoma (proposed by Weiss in 1963). Thus increased intraocular pressure with iris neovascularization and/or angle neovascularization appearing after ischemic central retinal vein occlusion (CRVO) is defined as neovascular glaucoma in vaso-occlusive retinopathy (Allingham et al. 2005).

Etiology

Ischemic central retinal vein occlusion is a frequent cause of neovascular glaucoma. The cumulative risk of ocular neovascularization in ischemic CRVO is about 70% for iris neovascularization, 60% for angle neovascularization, and 45% for neovascular glaucoma after 3 years of follow-up. In contrast to proliferative diabetic retinopathy, neovascularization at the disk (15%) and retina (10%) is rarely seen in ischemic CRVO. Hypoxia in areas of capillary non-perfusion causes neovascularization via angiogenic substances, mainly vascular endothelial growth factor (VEGF) produced by Müller cells (Hayreh 2005; Hayreh 2007).

In patients developing neovascularization after nonischemic CRVO, other causes of neovascularization such as diabetic retinopathy or ocular ischemia should be ruled out. Neovascular glaucoma may also be seen after central retinal artery occlusion, but only if ocular ischemia is the underlying cause.

Clinical Presentation

In the prerubeosis stage (early phases) after ischemic CRVO, the intraocular pressure may be normal or even reduced. The risk of neovascularization of the anterior segment is mainly dependent on the severity and extent (area) of retinal ischemia. Especially eyes with 30 or more disk areas of non-perfusion at fluorescein angiography are at risk. Fluorescein angiography of the iris reveals abnormal, leaking vessels in virtually all eyes with extensive retinal capillary closure. Also some patients with primary nonischemic CRVO may progress to ischemic CRVO. In the early preglaucomatous stage, slit-lamp biomicroscopy reveals dilated tufts of preexisting capillaries and fine, randomly oriented vessels on the surface of the iris near the pupillary margin. Gonioscopy may show a variable amount of angle neovascularization. In the open-angle glaucoma stage, typically occurring 8–15 weeks after the vascular occlusive event (therefore called 90-day glaucoma), there is florid rubeosis iridis, and the

aqueous reveals inflammatory reaction. By gonioscopy, the angle is still open, but the neovascularization may be intense. The IOP is elevated and may rise suddenly, and a hyphema may be present. In the angle-closure glaucoma stage, the stroma of the iris has become flattened, with a smooth, glistening appearance. Ectropion uvea is frequently present, and the pupil is often dilated. Gonioscopy shows peripheral anterior synechia leading eventually to total synechial closure of the chamber angle. The glaucoma in this stage is typically severe and usually requires surgical intervention (McIntosh et al. 2010).

Diagnostics

Various clinical tests have been evaluated to predict the severity of CRVO and thus the risk of anterior segment neovascularization. Besides visual acuity (VA) testing and ophthalmoscopy, manual kinetic perimetry (Goldmann), testing of relative afferent pupillary defects using neutral density filters, electroretinography (b-wave implicit time delay and a reduced b-wave/a-wave amplitude ratio), and fluorescein angiography have been used to predict the amount of retinal ischemia. The four functional tests (VA, visual fields, relative afferent pupillary defect, and electroretinography) are especially in early phases far more reliable than fluorescein angiography in differentiating nonischemic from ischemic CRVO. For detection of rubeosis iridis, careful slit-lamp examination and in doubt fluorescein angiography of the iris may help to differentiate dilated iris capillaries from neovascularization. Measuring of intraocular pressure and careful gonioscopy to differentiate between open-angle and angle-closure stage of neovascular glaucoma is mandatory.

Differential Diagnosis

All other causes predisposing to rubeosis iridis and neovascular glaucoma should be considered. They include all retinal ischemic diseases such as diabetic retinopathy, retinal detachment, hemorrhagic retinal disorders, Coats exudative retinopathy, Eales disease, Leber's congenital amaurosis, retinopathy of prematurity, persistent hyperplastic primary vitreous, sickle cell retinopathy, syphilitic retinal vasculitis, retinoschisis, Stickler syndrome, and optic nerve glioma with subsequent venous stasis retinopathy. Other causes such as irradiation retinopathy, intraocular tumors or lymphoma, and inflammatory diseases or surgically induced rubeosis and extraocular causes such as carotid artery obstruction or occlusion and fistula should also be considered to cause rubeosis iridis.

Prophylaxis

If ischemic CRVO is diagnosed, the severity and extent of retinal ischemia should be evaluated using the clinical findings and simple clinical tests. If severe ischemia is present, the risk of developing anterior segment neovascularization is high, and the patient should be monitored closely in the first 3–4 months. If any signs of rubeosis are detected or if there is increasing asymmetry in IOP readings, treatment is indicated. A prospective randomized trial has shown that prophylactic panretinal laser coagulation does not totally prevent anterior segment neovascularization and that prompt regression of the rubeosis is more likely to occur in response to photocoagulation in eyes that have not been treated previously.

Therapy

The first-line treatment is lowering of the IOP with topical or systemic medications, which may indirectly improve retinal perfusion. Suppression of angiogenesis by intravitreal or intracameral injection of anti-VEGF substances (ranibizumab, bevacizumab, or aflibercept) has been recently shown to significantly decrease anterior segment neovascularization. Reducing the oxygen demand of the retina by laser coagulation of the ischemic retina significantly reduces or eliminates anterior segment neovascularization. Laser treatment

should be applied primarily to the area of non-perfusion as panretinal photocoagulation has a negative effect on peripheral visual field. If medical IOP lowering is not effective enough, surgery (trabeculectomy or tube shunts) may be required. Surgically lowering IOP by trabeculectomy has been shown to be very effective in lowering the rate of recurrence of anterior segment neovascularization. When cloudy media precludes panretinal photocoagulation, transscleral panretinal cryotherapy often combined with cyclocryotherapy can control the IOP and reduce the neovascularization (Saito et al. 2010; SooHoo et al. 2015).

Prognosis

The majority of eyes may be saved using adequate treatment early enough in the disease process (before extensive angle-closure is present). Despite medical IOP lowering, intravitreal anti-VEGF injections and panretinal laser photocoagulation about 15–20% of eyes may be caught too late or not adequately respond to treatment and end up in absolute glaucoma or phthisis.

Epidemiology

CRVO may occur in a wide range of ages (14–92 years), but half of the patients are 65 or older. Ischemic CRVO is very rare in young patients. The overall prevalence of CRVO is 0.8 per 1000, which means that worldwide 2.5 million patients are affected. Assuming that only 20% of these CRVO are ischemic and only 45% are at risk of neovascular glaucoma, 225,000 patients are expected to suffer from neovascular glaucoma due to ischemic CRVO.

Cross-References

- ▶ Neovascular Glaucoma in Ischemic Central Retinal Vein Occlusion
- ▶ Neovascular Glaucoma in Proliferative Diabetic Retinopathy

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Neovascularization of the Retina

▶ Neovascularization, Retinal

Neovascularization, Retinal

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Synonyms

Neovascularization of the retina

Definition

Development of new blood vessels of a different kind or in an abnormal position, especially in tissues where circulation has been impaired by disease or trauma (Lee et al. 1998).

Etiology

Retinal ischemia causes release of angiogenic factors with the most common being vascular endothelial growth factor (VEGF). This, in turn, causes the development of new fine blood vessels.

Clinical Presentation

Retinal neovascularization presents as fine, irregular, fan-shaped, new vessels apparent on the optic disk or elsewhere on the retina. Initially blood vessels have minimal fibrous component and cross and extend beyond the internal limiting membrane. During later stages the vessels increase in size and extent with an increased fibrous component. They might contract and cause traction retinal detachment.

Diagnosis

Retinal neovascularization may be visible on clinical examination. Fluorescein angiography demonstrates a network of fine blood vessels with hyperfluorescence due to leakage.

Differential Diagnosis

1. Diabetic retinopathy
2. Retinal vein occlusion
3. Radiation retinopathy
4. Retinal vasculitis
5. Uveitis
6. Sickle cell retinopathy
7. Retinopathy of prematurity
8. Familial exudative vitreoretinopathy
9. Eales disease

Prophylaxis

In some conditions, such as retinopathy of prematurity, cryotherapy or laser ablation of ischemic retina may reduce oxygen demand, reduce the production of angiogenic factors, and as result prevent or reduce the growth of new retinal vessels (Cryotherapy for retinopathy of Prematurity Cooperative Group 2001; Early Treatment for Retinopathy of Prematurity Cooperative Group 2003).

Intravitreal injections of anti-VEGF drugs have also been shown to prevent the development of retinal neovascularization in diabetic retinopathy as well as in retinal vein occlusion (Brown et al. 2013).

Therapy

The purpose of treatment in cases with retinal neovascularization is to prevent complications that may cause visual loss such as vitreous hemorrhage or traction retinal detachment.

The mainstay of treatment for retinal neovascularization involves mainly the use of thermal laser photocoagulation in a pan retinal pattern to induce regression (Patz et al. 1981).

For patients with high-risk proliferative diabetic retinopathy (PDR), scatter panretinal photocoagulation (PRP) treatment is almost always recommended. The goal of scatter PRP is to cause regression of existing neovascular tissue and to prevent progressive neovascularization in the future. The amount of therapy necessary to achieve these endpoints is determined by the degree of regression of vessels.

Full pan retinal photocoagulation, as used in the Diabetic Retinopathy Study, included 1,200 or more 500 μm burns, separated from each other by one-half burn width, at 0.1 s duration. Treatments may be divided into two or more sessions (Patz et al. 1981).

Prognosis

Untreated retinal neovascularization may cause severe visual loss due to vitreous hemorrhage or traction retinal detachment, regardless of the etiology.

In proliferative diabetic retinopathy, the risk for severe visual loss was reduced by 50% in patients treated with laser PRP compared to untreated control eyes during a follow-up of over 5 years.

Epidemiology

A low estimate of the prevalence of proliferative diabetic retinopathy in a general population was reported at 0.3% in the Framingham Eye Study, representing at least 180,000 people (aged 52–85 years) in the USA with neovascularization. Other studies found the overall prevalence of all diabetic retinal neovascularization, including intraretinal microvascular abnormalities (IRMAs), to be 1.7% of the general population, representing 1.5 million Americans aged 43–84 years.

The incidence of retinal neovascularization associated with retinopathy of prematurity is estimated at 180,000 new cases per year in the USA.

A synthesis of the results of many studies shows that in the youngest category of premature newborns (born at 24–27 weeks of gestation), a neovascular stage of ROP occurred in 12–29% of the newborns; in the middle category (28–31 weeks of gestation), neovascular changes occurred in 2–20%; and in the oldest group (32–35 weeks of gestation), neovascularization was present in only 0–3.5% of infants.

In sickle cell retinopathy, approximately 27,580 (0.14% of adult African-Americans) have sickle cell anemia, and 25,610 (0.13%) have SC disease. It is estimated that the prevalence of neovascularization is 5,500 (20% of 27,580) cases of proliferative sickle retinopathy in African-Americans (aged 18–64 years) with sickle cell anemia.

Cross-References

- ▶ Central Retinal Vein, Occlusion of
- ▶ Diabetic Retinopathy
- ▶ Retinopathy of Prematurity

References

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Nerve Pain

▶ Postherpetic Neuralgia

Neural Tumor

▶ Neurofibromas, Discrete

Neurofibromas, Discrete

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Synonyms

Fibroma; Neural tumor

Definition

A benign tumor originating in peripheral nerve fibers.

Etiology

Neurofibromas on the eyelid and orbit can present as solitary neurofibroma, multiple localized neurofibromas, and plexiform neurofibroma. Multiple neurofibromas can be associated with neurofibromatosis type 1(NF-1), also called von Recklinghausen disease; plexiform neurofibroma is pathognomonic of this common autosomal dominant genetic disorder (NF-1). The solitary lesion is not associated with systemic disease.

Clinical Presentation

Neurofibromas (solitary or multiples) are flesh-colored lesions that can occur anywhere in the body. Lesions can present as circumscribed, but unencapsulated, masses deep in the subcutaneous plane to projecting as exophytic pedunculated papules. Their sizes also can vary greatly from small lesions 2–3 mm in diameter to larger growths several cm in diameter. Plexiform neurofibroma often presents as a diffuse infiltration of the eyelid and orbit. It produces the typical S-shaped curve and ptosis to the upper eyelid due to thickening and horizontal redundancy of this lesion. Cutaneous neurofibromas usually remain asymptomatic, but neurofibromas that develop in major peripheral or central nerves can cause motor or sensory dysfunction.

Diagnostics

Based on history, clinical examination, and confirmed by histopathological examination.

Differential Diagnosis

Differential diagnosis includes ▶ chalazion, malignant tumor, ▶ actinic keratosis, ▶ inverted follicular keratosis, and ▶ molluscum contagiosum.

Prophylaxis

Unknown

Therapy

Treatment depends on the site and extent of disease. Isolated cutaneous lesions may be easily surgical excised or just followed conservatively. Surgical debulking may be performed for plexiform neurofibromas if they become cosmetically unacceptable. Complete excision usually is impossible due to the infiltrative nature of these lesions.

Prognosis

Malignant degeneration of neurofibroma can occur in individuals with NF-1.

Epidemiology

Neurofibromas represent from 0.5–2.4% of orbital tumors. Plexiform neurofibromas are the most common form of benign neurogenic orbital tumor seen in children.

Cross-References

- ▶ Actinic Keratosis
- ▶ Chalazion
- ▶ Inverted Follicular Keratosis
- ▶ Molluscum Contagiosum

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Neuronal Ceroid Lipofuscinosis

► Ceroid Lipofuscinosis

Neuroparalytic Keratitis

► Neurotrophic Keratopathy

Neurosensory Retinal Detachment

► Subretinal Fluid

Neurotrophic Keratopathy

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Synonyms

Neuroparalytic keratitis

Definition

Neurotrophic keratopathy is a degenerative disease of decreased corneal sensitivity and healing, resulting from impaired corneal innervation (Bonini et al. 2003).

Etiology

Neurotrophic keratopathy may be caused by anything affecting trigeminal innervation of the cornea (Bonini et al. 2003). Common causes are herpes simplex and herpes zoster infections. Other causes include trigeminal neuralgia surgery, acoustic neuromas, topical anesthetics, and systemic diseases like diabetes.

Clinical Presentation

Neurotrophic keratopathy has been divided into three stages using the Mackie classification (Bonini et al. 2003).

Stage 1 – Patients present with nonspecific symptoms, including rose bengal staining of the inferior palpebral conjunctiva. Tear mucus viscosity is noted to increase, and dry spots may be found on corneal epithelium, suggesting future scarring and vascularization.

Stage 2 – A nonhealing corneal epithelial defect may result, with folding of Descemet's membrane, stromal swelling, and loosening of the surrounding epithelium.

Stage 3 – Progression of the disease to stage 3 continues if not limited at stages 1 or 2. This stage is associated with stromal melting, corneal ulcer, and perforation. The patient typically is asymptomatic though due to corneal denervation.

Diagnostics (Lab Diagnostics)

Clinical history is important for the diagnosis of neurotrophic keratopathy. Systemic diseases, such as diabetes, may lead to corneal trigeminal denervation (Groos 1997). Previous corneal surgeries also may contribute to corneal denervation.

A thorough cranial nerve exam is also necessary for the diagnosis of suspected neurotrophic keratopathy (Bonini et al. 2003). Brain neoplasms, such as acoustic neuromas, may involve the trigeminal nerve. Paresis of multiple nerves, such as CN III, IV, and VI, may suggest cavernous sinus involvement or aneurysm with associated trigeminal nerve involvement.

To successfully diagnose these patients, an accurate ocular examination is necessary. Corneal sensitivity tests for innervation and may be tested either with application of a cotton swab to the cornea or with a Cochet-Bonnet esthesiometer.

Slit lamp exam and dilated fundoscopy can reveal salient diagnostic information. Corneal scarring or epithelial changes may suggest prior infection, possibly herpes zoster or herpes

simplex. Examination of the eyelids may indicate blepharitis or exposure keratitis, factors known to be associated with neurotrophic keratopathy. Fundoscopy can also reveal signs of systemic disease, such as diabetic retinopathy.

To rule out bacterial, viral, or fungal etiology, corneal ulcers should undergo microbiological examination.

Differential Diagnosis

Differential diagnosis includes dry eye syndrome, blepharitis, chronic eye rubbing, exposure keratopathy, topical drug toxicity, ultraviolet keratopathy, mild chemical injury, contact lens-related disorders, corneal limbal stem cell deficiency, and infectious or immune cause for ulceration

Prophylaxis

Prophylactic antibiotics may be recommended if disease has progressed past initial stage (Groos 1997).

Therapy

Therapy is divided according to classification stages and must be initiated immediately to prevent progression (Groos 1997).

Stage 1 – Preservative-free artificial tears and ointment. Discontinue topical medications.

Stage 2 – Treat epithelial defect to prevent ulcers, prophylactic antibiotics, preservative-free artificial tears, and possible lateral tarsorrhaphy.

Stage 3 – Demands immediate attention in order to stop the stromal lysis and prevent perforation. In cases of stromal melting, topical collagenase inhibitors, such as *N*-acetylcysteine, tetracycline, or medroxyprogesterone, may be administered. Corneas that appear to be very thin despite lubrication and tarsorrhaphy often require cyanoacrylate glue and a bandage contact lens. Disease may still progress.

Prognosis

Neurotrophic keratitis remains one of the most challenging ocular diseases to treat. Patient prognosis depends upon several factors, such as etiology and degree of denervation (Bonini et al. 2003). The more severe the corneal denervation, the higher the likelihood of progression of the disease.

Since patients may remain asymptomatic, it is important for frequent check-ups with an ophthalmologist.

Epidemiology

Several etiologies exist for neurotrophic keratopathy, including infectious, iatrogenic, neoplasm, and drug-induced (Bonini et al. 2003). Herpes zoster (8% of patients) and herpes simplex are the most common causes of neurotrophic keratopathy.

Cross-References

- ▶ Blepharitis
- ▶ Dry Eye
- ▶ Exposure Keratitis/Keratopathy
- ▶ Herpes Stromal Keratitis

References

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Nevoid Basal Cell Carcinoma Syndrome

- ▶ Basal Cell Nevus Syndrome (Gorlin Syndrome)
- ▶ Gorlin Syndrome

Nevus Flammeus

► Port-Wine Stain (Nevus Flammeus)

Nevus Pigmentosus Systematicus

► Bloch-Sulzberger Syndrome (Incontinentia Pigmenti)

Nevus, Intradermal

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Synonyms

Acquired melanocytic nevus; Intradermal nevus; Melanocytic nevus

Definition

A type of nevus (benign neoplasms composed of nests of melanocytes) located exclusively within the dermis (Albert and Jakobiec 2008; Barnhill et al. 2004; Shields and Shields 2008).

Etiology

The cause is unknown. A genetic factor is likely in many families, working together with increased sun exposure. Usually present in childhood as small, flat tan macules that increase in size on the basal epithelium. As the lesion increases in diameter, a nest of cells drops into the dermis; later, the cells migrate entirely in the dermis. Therefore, the natural progression from junctional nevus to compound nevus, then to intradermal nevus may occur.

Clinical Presentation

Usually as elevated, fleshy, and slightly or moderately pigmented papules (light brown or flesh tone). Lesions vary in size from a few millimeters to a centimeter. They are frequently raised, dome-shaped, nonpigmented nodules, most commonly seen on the face (Fig. 1). There are some overlying telangiectatic vessels, and outgrowth of one or two coarse terminal hairs is common.

Diagnostics

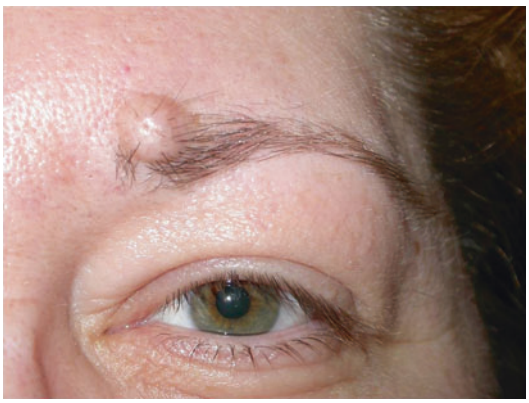
Usually by clinical presentation. Histopathologic evaluation is confirmatory (Barnhill et al. 2004).

Differential Diagnosis

Differential diagnosis includes ► melanoma, ► basal cell carcinoma, ► neurofibroma, tricoepithelioma, and ► verruca vulgaris.

Prophylaxis

Avoidance of sun exposure and sun education.



Nevus, Intradermal, Fig. 1 Dome-shaped nevus on the left medial eyebrow

Therapy

The majority do not require treatment and can be observed periodically. Indications for removal include cosmetic concerns, chronic irritation (itching and/or bleeding), and changes in appearance (color, size, or shape) that are suspicious for melanoma. Options of surgical therapy when the lesion involves eyelids include shave biopsy, excisional biopsy, or full thickness eyelid biopsy (Albert and Jakobiec 2008).

Prognosis

Most are benign with little malignant potential. The most active nevus is the junctional nevus. As nevi descend further into the dermis (compound and intradermal nevi), they decrease their potential to malignant transformation.

Epidemiology

Benign pigmented nevi in adults are most commonly intradermal. The prevalence of melanocytic nevus varies with age and race. They increase in number gradually during childhood and adolescence, reaching a peak during adult life and declining with increasing age. These lesions are common in patients with light or fair skin (Albert and Jakobiec 2008; Barnhill et al. 2004; Shields and Shields 2008).

Cross-References

- Basal Cell Carcinoma of Eyelid
- Choroidal and/or Ciliary Body and/or Iris Melanoma
- Compound Nevus
- Excisional Biopsy
- Full-Thickness Eyelid Biopsy
- Junctional Nevus
- Neurofibromas, Discrete
- Verruca Vulgaris

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Nevus, Junctional

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Synonyms

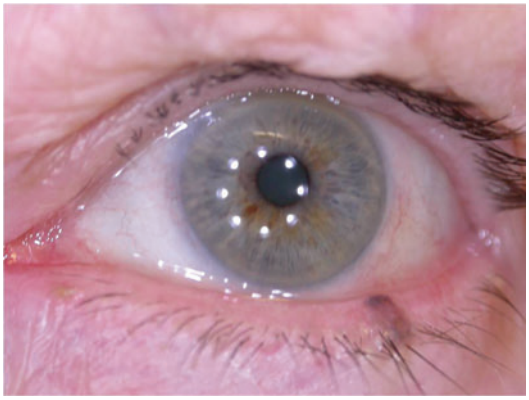
Acquired melanocytic nevus; Junctional nevus; Melanocytic nevus

Definition

A type of nevus (benign neoplasms composed of nests of melanocytes) located at the dermoepidermal junction.

Etiology

Unknown, but a genetic factor is likely and increased sun exposure may be a risk factor. They may occur on the eyelid skin and on the eyelid margins. Lesions typically present in childhood as small, flat tan macules that increase in size on the basal epithelium. As the lesion increases in diameter, a nest of cells drops into the dermis; later, the cells migrate entirely in the dermis. Therefore, the progression from junctional nevus to compound nevus, then to intradermal nevus may occur (Barnhill et al. 2004; Albert and Jakobiec 2008; Shields and Shields 2008).



Nevus, Junctional, Fig. 1 Pigmented melanocytic nevus on margin of lower eyelid

Clinical Presentation

Generally flat or slightly elevated, round or oval macules with uniform pigmentation. Their color ranges from medium to dark brown (Fig. 1).

Diagnostics

Clinical presentation. Histopathologic evaluation is confirmatory to junctional nevus.

Differential Diagnosis

Differential diagnosis includes ▶ melanoma, ▶ lentigo senile, lentigomaligna, ▶ atypical nevus, and ▶ freckles.

Prophylaxis

Avoidance of sun exposure and sun education.

Therapy

The majority of common acquired melanocytic nevi do not require treatment and can be observed periodically. Indications for removal include cosmetic concerns, chronic irritation (itching and/or bleeding), and changes in appearance (color, size, or shape) that are suspicious for melanoma. Options of surgical therapy when the lesion involves eyelids includes shave biopsy, excisional biopsy, or full thickness eyelid biopsy.

Prognosis

Most are benign with little malignant potential. The most active nevus is the junctional nevus. As nevi descend further into the dermis (compound and intradermal nevi), they decrease in potential for malignant transformation.

Epidemiology

The prevalence of melanocytic nevus varies with age and race. They increase in number gradually during childhood and adolescence, reaching a peak during adult life and declining with increasing age. These lesions are common in patients with light or fair skin (Barnhill et al. 2004; Albert and Jakobiec 2008; Shields and Shields 2008).

N

Cross-References

- ▶ Compound Nevus
- ▶ Choroidal and/or Ciliary Body and/or Iris Melanoma
- ▶ Excisional Biopsy
- ▶ Freckle
- ▶ Full-Thickness Eyelid Biopsy
- ▶ Intradermal Nevus
- ▶ Lentigo Senile (Liver Spots)

References

Albert D, Jakobiec F (2008) Principles and practice of ophthalmology, 3rd edn. Saunders, Philadelphia, p 3367

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Nexacryl

► Cyanoacrylate Adhesive

Night Blindness

► Nyctalopia: Night Blindness

No-Anesthesia Cataract Surgery

► Anesthesia, Cataract

Nodular Cell Hidradenoma

► Hidradenoma, Clear Cell (Eccrine Acrospiroma)

Nodular Corneal Dystrophy in Tropical Arid Countries

► Keratinoid (Spheroidal) Degeneration
► Keratopathy Actinic (Labrador Keratopathy/ Spheroidal Degeneration)
► Spheroidal Degeneration

Nodular Hyaline

► Keratinoid (Spheroidal) Degeneration

Nodular Hyaline, Band-Shaped Keratopathy

► Keratopathy Actinic (Labrador Keratopathy/ Spheroidal Degeneration)

Nodular Oncocytosis

► Oncocytoma

NOE Fractures

► Naso-Orbital-Ethmoid Fractures

Nonarteritic Anterior Ischemic Optic Neuropathy

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Synonyms

NAION; NA-AION

Definition

Non-arteritic anterior ischemic optic neuropathy (NAION) is characterized by a sudden, typically

painless, loss of vision in one eye and a swollen optic disc. Although typically unilateral, bilateral, and sequential, also rarely bilateral, simultaneous NAION can occur. Typically, affected and fellow eyes with NAION demonstrate a small optic nerve cup-to-disc ratio (i.e., the "disc at risk"). There must be optic disc edema on acute presentation in NAION (i.e., anterior optic neuropathy), although chronic and resolving cases may demonstrate optic atrophy and/or sector pallor. The disc edema often presents in a sectoral fashion, although many cases show diffuse edema.

NAION is a presumed ischemic event occurring at the anterior optic nerve (at the level of the lamina cribrosa). There should not be any concomitant retinal or significant choroidal ischemia, and if more than one blood supply affected, an alternative diagnosis (such as ▶ arteritic anterior ischemic optic neuropathy or ▶ giant cell arteritis (GCA)) should be suspected.

Initially localized ischemia of the optic nerve head may result in further ischemia in a patient with no room to expand within the lamina cribrosa (i.e., the "crowded disc at risk"). This "compartment syndrome" might result in further vascular compromise and progressive ischemia. The process eventually results in axonal damage and corresponding ganglion cell death, leading to a corresponding visual field defect.

Etiology

As noted above, a small optic nerve/small cup-to-disc ratio may predispose to the development of NAION after a relatively mild ischemic event to the optic nerve head. Up to 97% of the cases of NAION involve a small optic disc (less than 1.2 mm) with a small or absent physiological cup (0.2 or less).

Additional predisposing risk factors for NAION include vasculopathic conditions (e.g., hypertension/hypotension, hyperlipidemia, cardiovascular disease, atherosclerosis, or diabetes mellitus). Other less common risk factors include hypercoagulable states, anemia, high altitude, sleep apnea, certain medications such as vasodilators (phosphodiesterase-5 inhibitors), high intraocular pressure (which decreases ocular perfusion), renal dialysis, general surgical procedures, iatrogenic hypotension (often nocturnal), and malignant hypertension.

Clinical Presentation

NAION typically presents with acute, monocular, painless, visual field loss. The visual acuity may be normal (up to 50%) or decreased and the severity is quite variable. Typical NAION however does not usually result in light perception (LP) or no light perception (NLP) vision and this scenario should prompt consideration for alternative etiologies including giant cell arteritis (GCA)-related arteritic AION (AAION).

The majority of patients with NAION have a nerve fiber layer visual field defect (commonly inferior altitudinal or inferotemporal field defect), but some have concomitant central visual field loss. Dyschromatopsia is also common in the affected eye. A relative afferent pupillary defect this scenario should be present in unilateral cases but may be absent if bilateral and symmetric afferent disease is present. Posterior segment exam usually reveals sector or diffuse disc edema, and the fellow eye should reveal a small cup-to-disc ratio.

Diagnostics

In patients over the age of 50 years, it is imperative to consider giant cell arteritis (GCA) or arteritic anterior ischemic optic neuropathy (AION). Fluorescein angiography can be performed to evaluate the retinal and/or choroidal circulation in cases suspected of having GCA.

Evaluation

Typical NAION does not usually require extensive testing. Because NAION is not usually an embolic disease, cardiac and carotid evaluations are not necessary unless indicated for other purposes. Evaluation and management of typical vasculopathic risk factors (e.g., hypertension,

diabetes, hyperlipidemia, discontinuation of smoking, sleep apnea) are recommended.

Differential Diagnosis

1. Arteritic anterior ischemic optic neuropathy (AION)
2. Optic neuritis
3. Amiodarone optic neuropathy
4. Posterior ischemic optic neuropathy (PION)
5. Leber hereditary optic neuropathy

Prophylaxis

Treatment of predisposing factors (diabetes, heart disease, hyperlipidemia, anemia, sleep apnea) and prevention of precipitating factors (hypotension, decreased oxygen saturation, increased intraocular/episcleral pressure) may reduce the incidence of NAION in the fellow eye, but there is no head-to-head trial evaluating these recommendations. Daily aspirin is sometimes recommended, but has conflicting reports as to its efficacy in preventing NAION in the partner eye.

Therapy

Oral prednisone treatment remains controversial regarding its efficacy in NAION. Hayreh et al. found an improvement in visual acuity in 69.8% ($n = 236$) of treated eyes versus 40.5% ($n = 301$) of untreated eyes in a non-blinded prospective study (p-0.001), whereas in a 36-patient study (treatment $n = 9$, control $= 27$), Rebolleda et al. found no statistical significance in visual acuity, median deviation on automated Humphrey visual fields, or retinal nerve fiber layer thickness on Stratus optical coherence tomography. Thus, controversy remains within the neuro-ophthalmic community concerning the use of corticosteroids in acute NAION, and the decision to treat with prednisone should be made on a case-by-case basis.

In the ischemic optic nerve decompression trial (IONDT), optic nerve sheath fenestration was not shown to be helpful in nonprogressive NAION, and in fact, the authors concluded they were harmful and should not be performed in this disease. Hyperbaric oxygen therapy has also not been shown to be effective. Aspirin may have a role in preventing NAION in the partner eye (conflicting data), but has not been shown to be efficacious in the affected eye. In addition, use of aspirin in the acute phase of NAION has not been studied. Tissue plasminogen activator has not been studied in NAION, but because the disease is thought to be caused by small vessel ischemia and not a thromboembolic or thrombotic etiology, this would not be a treatment of choice.

Prognosis

Roughly 40% of patients with NAION experience some improvement in their visual acuity in the months to years following their initial ischemic insult. These changes generally stabilize over 6 months from the time of initial insult. There is not a strong correlation in the severity of NAION between one eye and the fellow eye. NAION can occur in approximately 15% of contralateral eyes but typically does not recur in the same eye (<5%). Presumably as atrophy of the axonal nerve fibers occurs, this may create more room within the crowded cup, acting as a protective factor against a recurrent attack in the same eye.

Cross-References

▶ Arteritic Anterior Ischemic Optic Neuropathy
▶ Diabetic Disc Edema
▶ Optic Neuropathy

Further Reading

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Nonarteritic PION (NA-PION)

► Posterior Ischemic Optic Neuropathy

Noninfectious Keratitis with Ulceration

► Ulcerative Keratitis Disease

Nonius Acuity

► Hyperacuity (Vernier Acuity)

Nonnecrotizing Keratitis

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Synonyms

Herpes stromal keratitis

Definition

Herpes stromal keratitis (HSK) can present in necrotizing and non-necrotizing forms. Non-necrotizing keratitis results when inflammation of the cornea occurs in the absence of an infectious virus, usually leaving the epithelium unaffected. It is likely that the two types of HSK simply represent a spectrum of disease rather than two diseases with distinct pathologies.

Etiology

HSK usually results from infection by the herpes simplex virus type 1 (HSV-1) in adults and HSV-2 in neonates, though changing sexual behavior patterns are making HSV-2 an increasingly more common cause in adults. Primary infection especially with HSV-1 arises from exposure to active lesions or virus-laden secretions of close contacts, or more commonly as a secondary site of recurrence. In the former situation, the primary infection can cause a painful lesion that mainly affects the corneal epithelium and lasts for several days or weeks. The condition resolves without permanent damage to the cornea but remains uncured as the virus persists in the ophthalmic branch of the trigeminal ganglia in a dormant state known as latency. In the case that the infection occurs as a secondary site of recurrence, primary infection affects sites innervated by the facial nerve, but when the latent virus reactivates in the trigeminal ganglion, spread to the ophthalmic division may occur, leading to ocular recurrence.

Recurrent lesions often develop into a chronic immunoinflammatory event, termed herpes stromal keratitis. The exact mechanisms by which latency is established, maintained, and revoked are currently poorly understood and represent an active area of research. Most often, the immune-mediated response to nonreplicating virus involves the epithelium but, ultimately, the stroma becomes the main site for inflammatory reaction, edema, angiogenesis, permanent scarring, and impaired vision. If left unattended, corneal ulceration and perforation, or even blindness, may ensue. Non-necrotizing keratitis encompasses these inflammatory events in the cornea that are not explained by a reaction to live viral particles in the corneal stroma.

Clinical Presentation

Pain in the affected eye is the most common. Both inflammatory and reparative events are visible by slit lamp. Cellular infiltration, neovascularization, and scarring may be present as well, with stratified opacities and corneal lamellae leading to stromal opacity. While corneal necrosis and ground-glass appearance of the stroma may be apparent for necrotizing keratitis, the non-necrotizing form should only exhibit varying degrees of corneal scarring, facet formation, and perforation.

Diagnosis

Accurate diagnosis can be made by demonstrating HSV in the corneal tissue samples or ocular secretions by cell culture, by immunofluorescence staining, or by detecting the viral genome through polymerase chain reaction (PCR). Despite PCR's advantages as the most rapid, sensitive, and specific method, high cost often limits the use of the procedure to research centers. Serological diagnosis can confirm a primary infection, but is not useful since the majority of the population is seropositive, including those who experience recurrent lesions.

Differential Diagnosis

Abrasions
Bacterial, chlamydial, parasitic, or fungal keratitis
Graft rejection following keratoplasty
Zoster caused by varicella zoster virus

Prophylaxis

Developing an effective prophylactic or therapeutic vaccine for HSK has been pursued strongly but with no real success to date. The most targeted HSV-induced diseases are genital infections caused by HSV-2, as these are much more common than ocular issues. If the development of the HSV-2 vaccine is successful, this could help reduce the incidence of neonatal ocular herpes. For adults, the more serious clinical consequences of ocular HSV infection arise from recurrences, which often have an immunopathological component. Therapeutic vaccines could make the condition worse rather than better, requiring further examination of the issue to assure safe development of therapeutic vaccines.

Therapy

Treatment of non-necrotizing keratitis addresses the fact that stromal disease is an immune response to viral antigen. Steroid therapy is used to control inflammation, and antivirals may be administered to help reduce the chances of recurrence in general. Typical steroid treatment starts at the lowest therapeutic dose and can be reduced slowly over weeks or even months, but if inflammation recurs, it should be increased.

Prognosis

Prompt and appropriate treatment may minimize the risk of scarring, which represents the major cause of morbidity from corneal HSV infection.

Epidemiology

Herpetic keratitis is the most common infectious cause of impaired vision in adults in the developed world. The disease exhibits no gender bias, and any genetic factors that increase susceptibility are poorly understood.

Cross-References

- ▶ Bacterial Keratitis
- ▶ Disciform Keratitis, Herpes Simplex Virus Causing
- ▶ Interstitial Keratitis
- ▶ Keratitis
- ▶ Necrotizing Keratitis

- ▶ Sclerokeratitis
- ▶ Stromal Keratitis (Herpetic)

Further Reading

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Nonorganic Ptosis

- ▶ Pseudoptosis

Nonorganic Visual Loss

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Synonyms

Functional; Hysterical amblyopia; Malingering; Psychogenic; Visual conversion

Definition

Nonorganic vision loss (NOVL) is defined as visual dysfunction that cannot be attributed to an organic, anatomic, or physiological cause and is incompatible or inconsistent with the objective findings. Unfortunately, organic and NOVL are not mutually exclusive and can occur in the same individual and the presence of nonorganic overlay does not preclude the development of organic disease.

Etiology

The actual etiology of NOVL is variable and can be due to deep-seated psychological conflict manifesting unconsciously as NOVL or may be purposeful for secondary gain (malingering). Some patients with NOVL meet the Diagnostic and Statistical Manual of Mental Disorder V (DSM V) criteria for malingering, conversion disorder, factitious, or somatization disorders, but in our experience most patients do not have a clear underlying psychiatric diagnosis or any defined trigger apart from generalized psychosocial stress or nonspecific anxiety or depression. In addition, NOVL is common as an overlay in patients with organic disease.

Clinical Presentation

Patients with NOVL may present in a variety of ways. The most common presenting symptom in NOVL is loss of visual acuity and the second most common is visual field loss. The loss in acuity or visual field may range from mild to moderate, could be unilateral or bilateral, transient or constant. Visual field defects range from a constricted visual field (i.e., tunnel or spiral fields) to diffuse constriction. Less commonly a central scotoma may be the presenting visual field defect to have NOVL, and the presence of a central scotoma or homonymous or bitemporal hemianopsia should be considered to be organic until proven to be NOVL. Other less common symptoms of NOVL

are distorted shapes, abnormal colors, and positive visual phenomenon (e.g., seeing dots or snow, and lines). Most patients with NOVL have isolated visual complaints, but other nonorganic neurologic symptoms and signs may also be present (e.g., pseudoseizures, unexplained weakness or paresthesias, unexplained eye pain or headache).

Diagnostics

The key to making the diagnosis of NOVL is first to complete a thorough history and physical examination to exclude organic etiologies. As noted above, it is also important to keep in mind that both NOVL and an organic disease occurring together (i.e., nonorganic overlay).

The duty of the ophthalmologist in NOVL is to:

1. Prove that the patient has a normal ocular examination and does not show any organic or physiological cause that could account for the patient's symptoms.
2. Demonstrate that the patient has a better visual acuity and or visual field than claimed proving that there is NOVL.

There are several tests that had been designed for testing NOVL. The choice of the best test to use depends on the clinical presentation, laterality, severity, and type of NOVL.

In monocular visual acuity loss with a normal or near normal fellow eye, a monocular vertical prism test using a 4-prism diopters base down vertical prism can be placed in front of the unaffected eye, see Fig. 1. Prior to the test you should explain to the patient that you are going to "test the good eye first" and that the prism will split the image and will produce double image. For instance, a patient with VA 20/20 in the right eye (OD) and 20/100 in left eye (OS) should have the 4-prism diopters base down placed in front of the good eye (OD). A 20/40 single Snellen letter is then shown to the patient with both eyes open but with the prism over the "good eye" (OD). An organic 20/100 OS should produce the response that the patient sees only one 20/40 letter. However, in a case of NOVL the patient will report seeing two vertically displaced letters. This result helps to prove two points: first the nonorganic nature of the vision loss and the second it is an objective way to measure VA in the "bad eye" and prove at least 20/40 vision OU. The duochrome test is another useful method in testing for NOVL. The patient wears red-green glasses and then is shown the Snellen chart with the duochrome test option (i.e., red and green halves of the Snellen line or chart). The green lens should only see the one side of the chart (green). The downside of this test is that the patient can easily figure out which eye is being tested by closing either eye. Fogging is another test that is commonly used but again is susceptible to being defeated by the astute malingerer who closes either eye prior to the testing to determine the "correct" organic response. To perform this test you first will test the VA in both eyes. Then gradually add lenses of progressively higher

Nonorganic Visual Loss, Fig. 1 NOVL a 4-prism diopters base down prism can be placed in front of the unaffected eye

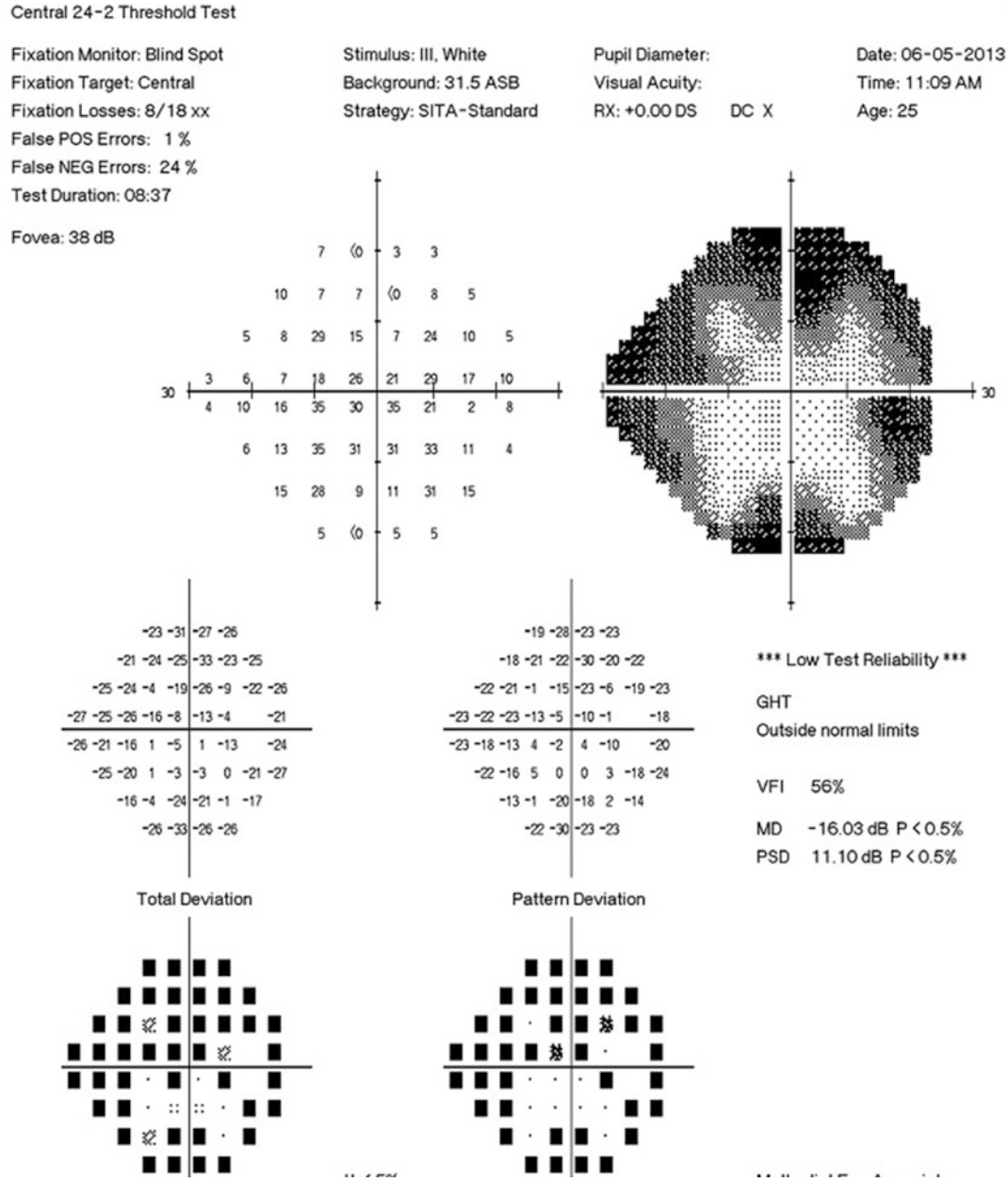
power in front of the good eye. This will gradually blur the vision in the good eye and may allow you to determine the actual acuity of the claimed "bad" eye. An alternative way to perform this fogging test is by using rotating spheres in the "bad eye" and rotating cylinders in the "good eye" to confuse the patient and distract them from detecting the fogging of the "good eye" and force the patient to read the chart with the supposedly visually impaired contralateral eye. Fogging tests often, however, reveal the clinicians' attempts to disprove the visual loss as organic and more subtle testing of NOVL are generally superior.

In a case of binocular VA loss, stereopsis testing can be used to test for NOVL since stereoacuity correlates well with VA. A common example of this is the fact; 40 s of arc of stereoacuity is equivalent to 20/20 visual acuity in both eyes. Standardized tables comparing stereoacuity to projected binocular visual acuity in each eye are available. Color vision testing likewise can be a very useful test in case of binocular VA loss. If the patient is able to correctly identify all of the Ishihara plates this is strong but not absolute evidence against an optic neuropathy as the cause of the degraded visual acuity.

In contrast to cases of mild to moderate visual loss, patients claiming severely impaired vision to light perception or no light perception the tests are easier to deploy to detect NOVL. Proprioception test can be used by asking the patient to touch the right index finger to the left index finger of their hands with both eyes open and with the "good eye" patched. Failures to perform accurate propioceptive tasks (which of course do not require vision) are suggestive of NOVL. The mirror test can be used in patients with monocular or binocular vision severe visual loss (e.g., claimed LP or NLP vision). The test is performed by placing a large mirror close enough to the patient so that they cannot look past it and then rotating the mirror from side to side. If the patient has NOVL their eyes will follow the reflection of their face in the mirror as it moves. Performing the test binocular conditions and then covering the supposed "good eye" should continue to elicit the eye movement in response to the mirror in the "bad eye" suggesting NOVL. In patients with bilateral severe visual loss (e.g., LP or NLP) the mirror test can be performed with both eyes open. As mentioned this test is only useful if the claimed level of visual loss is severe. Therefore, it should not be used if the vision loss is better than 20/200 to counting fingers vision because the test is not valid as the patient might still organically be able to see their face in the mirror. Visual threat test can be used in LP or NLP vision cases using a threatening hand motion towards the patient in an attempt to induce a blink, or withdrawal response which would indicate NOVL. We do not like this test as it involves a threatening motion and could be misinterpreted by the patient or their family if organic visual loss is present and could also provoke an unwelcome or unintentional negative patient response that might damage the legitimate patient-doctor relationship. An optokinetic nystagmus (OKN) drum can be used to demonstrate the physiological response of nystagmus in a supposedly blind eye under monocular or binocular conditions. The presence of an OKN nystagmus in an involved eye(s) with severe visual loss would be a clue suggesting NOVL.

As mentioned previously the majority of NOVL patients claiming a visual field defect describe a constricted visual field in one or both eyes. The constricted visual field or "tunnel field" that is usually present with NOVL can usually be differentiated from a constricted field due to an organic cause, see Fig. 2. The "tunnel field" present in NOVL can be tested for using a tangent screen or with confrontation testing at 1 m and 2 m. The constricted visual field due to an organic cause typically expands at 1 m and 2 m testing demonstrating a "funnel" expansion. In contrast, patients with NOVL do not present with this expansion and instead have a "tunnel field," see Figs. 3 and 4.

Another test for a patient claiming to have a severely reduced visual field is saccade testing into the supposedly blind visual field. When performing this test it is important to instruct the patient that you are testing eye movements (ocular motility). The patient is instructed to look at a primary target such as the examiners nose and then make a saccade to a peripheral target like the examiner's hand or finger which is placed in a claimed blind area of their VF. If the patient is able to make this saccadic movement quickly and



Nonorganic Visual Loss, Fig. 2 NOVL with constricted ("cloverleaf") visual field

accurately, then this is evidence of NOVL. If the cause was organic the patient would not be able to make an accurate saccade to the target in the blind field and instead might use roving or searching movements to find the target. In some cases, patients will tell the examiner they cannot see the peripheral target and thus cannot make the eye movement. In this case the examiner should tell the patient to "use their intact central vision" to look directly at the target. Another way to demonstrate NOVL is if a patient is claiming to have a monocular visual field loss with the other

Nonorganic Visual Loss, Fig. 3 NOVL confrontation testing at 1 m

Nonorganic Visual Loss, Fig. 4 NOVL confrontation testing at 2 m

eye being normal is by testing the visual field with both eyes open. Since the nasal and temporal portions of each visual hemifield overlaps that of the other eye, maintaining the monocular visual field defect under binocular testing conditions would indicate NOVL.

Electrophysiological testing such as full-field ERG or multifocal electroretinogram (ERG) and visual-evoked potential (VEP) may help to exclude other organic causes or confirm NOVL in difficult cases. Other newer tests such as pupil perimetry with normal pupil response could be used to detect NOVL.

Differential Diagnosis

Organic versus NOVL; NOVL with organic visual loss (nonorganic overlay); psychiatric disorders (e.g., conversion disorder, somatization) versus secondary gain (e.g., malingering).

Prophylaxis

Non applicable.

Therapy

The mainstay of treatment of NOVL is to reassure them there is no serious visual pathway diseases causing their symptoms, there is no brain or eye pathology that may lead to blindness, and that a full visual recovery should be expected. In pediatric cases, it is very important that the parents understand the presence of the NOVL and to identify and treat any psychosocial stressors or secondary gain. It is also very crucial to instruct them not to punish their child for the NOVL as this response might hinder recovery and does not allow the child an "easy way out." This philosophy is similar for adults with NOVL as getting

angry or confrontational with the malingering patient will not help and doing so with a conversion disorder patient will not alleviate their deep-seated psychological drivers. We recommend instead providing these patients with reassurance that the issue will resolve. Although psychiatric evaluation may be considered in some cases of NOVL, most patients do not meet any specific DSM V diagnosis. We prefer the use of the term NOVL in ophthalmology over specific DSM V diagnosis codes as these diagnoses are probably left to psychiatrically trained providers.

Prognosis

The visual prognosis is usually excellent in the majority of cases. Most cases of NOVL spontaneously improve within a year after presentation with NOVL. Nevertheless, improvement may be very slow and incomplete in a minority of patients. There is no clear consensus about factors that may influence the visual outcome in cases of NOVL and who will be under the risk of a poor visual recovery.

Cross-References

▶ Malingering
▶ Psychogenic

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Nonsteroidal Anti-inflammatory Agents

▶ Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

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Synonyms

Nonsteroidal anti-inflammatory agents; NSAIDS

Definition

Nonsteroidal anti-inflammatory drugs are a heterogeneous group that block COX enzymes and reduce prostaglandin production. They have analgesic, antipyretic, and anti-inflammatory effects. In addition, some NSAIDs prevent platelet aggregation, which can lead increased bleeding time.

Indications

This group of drugs is used in the treatment of acute and chronic pain, inhibition of platelet aggregation, and reduction of fever. Although most NSAIDs possess anti-inflammatory properties others, such as acetaminophen, do not display clinically significant effects. Topical flurbiprofen is used to prevent papillary constriction during intraocular surgery.

Contraindications

Oral nonsteroidal anti-inflammatory agents are contraindicated in patient with a history of allergic

reaction to aspirin or aspirin-like products. They should also be used with caution in individuals with severe asthma and congestive heart failure. They should be avoided in patients with kidney failure, liver diseases, bleeding disorders, gastrointestinal ulcers, and gastroesophageal reflux disease. In addition, salicylates are contraindicated in children and teenagers with viral illnesses.

Topical nonsteroidal anti-inflammatory agents are contraindicated in patients with dry eye syndrome and dendritic epithelial herpes simplex.

Use and Dosage

Oral NSAIDS are used to treat mild to moderate pain, fever, and inflammation due to musculoskeletal disorders. Acetaminophen, which belongs to the para-aminophenol derivative class of NSAIDs, has analgesic and antipyretic effects but lacks significant anti-inflammatory properties.

Flurbiprofen, a topical NSAID, is commonly used to reduce pupillary constriction during intraocular surgery. Topical NSAIDS are also used to treat postoperative inflammation and cystoid macular edema.

Adverse Reactions

A common adverse effect of oral NSAIDSs is gastrointestinal irritation, which can lead to ulcers. Development of ulcers can lead to gastrointestinal bleeding with subsequent anemia. Certain classes of NSAIDs inhibit platelet aggregation and increase bleeding. Salicylates have the potential to cause acute renal failure in patients with chronic renal disease, congestive heart failure, liver disease associated with ascites, dehydration secondary to diuretics, and in patients with hypotension due to acute hemorrhage.

The use of salicylates in children and teenagers with viral disease has been associated with the development of Reye syndrome.

Topical NSAIDs can lead to stinging and have been associated with delayed surface healing, sterile corneal melts and perforations.

Interactions

The use of non-aspirin NSAIDs and aspirin as well as the combination of corticosteroids and NSAIDs increases the potential for gastrointestinal irritation and ulcers and increases the risk of bleeding. NSAIDs may attenuate the effect of ACE inhibitors. The combination can also lead to bradycardia and syncope in the presence of hyperkalemia. This is particularly true in patients with hypertension, diabetes mellitus, and ischemic heart disease. NSAIDs interfere with warfarin metabolism, which leads to increase levels of the drug. In addition, NSAIDs inhibit platelet aggregation and when given with warfarin lead to increased bleeding time.

Cross-References

▶ Aspirin: Usage, Effects, and Dosage in Ophthalmology

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Nonstigmatic Refraction

▶ Refractive Astigmatism

Nonsyphilitic Interstitial Keratitis

▶ Cogan Syndrome

Nontuberculous *Mycobacteria* Keratitis

► Mycobacterium chelonae Keratitis

Nonulcerative Keratitis

► Interstitial Keratitis

NPS

► Onychoosteodysplasia (Nail-Patella Syndrome)

NPS1

► Onychoosteodysplasia (Nail-Patella Syndrome)

NSAIDS

► Nonsteroidal Anti-inflammatory Drugs (NSAIDs)

Nuclear Fragments

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Synonyms

Nuclear remnants

Definition

During modern cataract surgery, the crystalline lens is divided into smaller fragments which are removed from the eye by phacoemulsification and aspiration. Fragments of the nucleus that remain in the eye may give rise to complications such as prolonged inflammation, cystoid macular edema, and elevation of intraocular pressure (Vajpayee et al. 2001).

Epidemiology

There are no figures about incidence. In a large retrospective review of charts over a time frame of 13 years (Hui et al. 2006), 16 cases of retained nuclear fragments without posterior capsular rupture could be identified.

History

The history of retained nuclear fragments causing problems is linked with the history of phacoemulsification. Normally, during previously used cataract extraction techniques such as extra- and intracapsular cataract extraction (ECCE and ICCE), nuclear fragments are not produced.

Clinical Features

Nuclear fragments in the anterior chamber are often small and could be identified as yellowish chips. Sometimes, gray iris color, a pronounced arcus senilis, and corneal edema may cause difficulties of identifying nuclear fragments. At later stages, a prolonged inflammation raised intraocular pressure and corneal edema and probably a cystoid macular edema occur if nuclear fragments are retained in the anterior chamber. If such symptoms occur without visible fragments, a remnant trapped behind the iris or in the zonula should be suspected.

A rent in the posterior capsule bears the risk of descent of nuclear fragments into the vitreous

cavity (Vajpayee et al. 2001). Although this complication is dreaded and the surgeon's vigilance during phacoemulsification is focused on protecting the posterior capsule, sometimes the loss of smaller fragments into the vitreous remains unnoticed.

Tests

Prolonged inflammation and persistent corneal edema should raise suspicion of retained nuclear material. In those eyes, careful slit lamp examination is needed. Sometimes only gonioscopy can reveal small retained nuclear chips. Early after rupture of the posterior capsule, a fundus exam through the dilated pupil is necessary to rule out retained lens fragments and retinal tears. In the presence of corneal edema, an ultrasound examination may be helpful. Eyes with present or suspected retained nuclear fragments must be monitored closely for hypertension and subsequent glaucoma.

Differential Diagnosis

Although the appearance of nuclear fragments is unique, there may be similarities to other lens material such as cortex or epinuclear remnants.

Etiology

A fragmentation of the nucleus into many smaller chip-like pieces during phacoemulsification increases the risk of retained fragments in the anterior or posterior chamber. Retained nuclear fragments have been observed more frequently in myopic eyes, they probably get trapped in the relatively spacious posterior chamber in those eyes (Hui et al. 2006). Corneal edema, a pronounced arcus lipoides, and gray iris color can cause difficulty of visualization of nuclear fragments during and after phacoemulsification. The rupture of the posterior capsule during phacoemulsification bears a high risk of descent of nuclear fragments into the vitreous.

Treatment

Retained fragments in the anterior chamber should be removed with an irrigation/aspiration system as early as possible. If inflammation is already present, increase of the local steroid dose and systemic steroids can be helpful. While small nuclear fragments in the vitreous cavity can be observed and treated with systemic and local steroids, pars plana vitrectomy and removal is required if the fragments are larger.

Prognosis

The prognosis depends on complications like secondary glaucoma, cystoid macular edema, and corneal decompensation. If remaining fragments are removed from the eye before such complications develop, prognosis is good.

Cross-References

- ▶ Phacoemulsification and Posterior Chamber Intraocular Lens (IOL) Implantation
- ▶ Posterior Capsule Rupture

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Nuclear Remnants

▶ Nuclear Fragments

Nutritional Amblyopia

- ▶ Toxic/Nutritional and Hereditary Optic Neuropathy
- ▶ Toxic Optic Neuropathy

Nyctalopia: Night Blindness

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Synonyms

Night blindness

Definition

Decreased or impaired vision in dark environments due to absence or subnormal activity of rod photoreceptors.

Etiology

Many causes of nyctalopia exist. Potential etiologies can be divided into five different groups of disorders:

Group 1: Congenitally Inherited Diseases

Congenital stationary night blindness (CSNB) refers to a distinct group of diseases that are both genetically and phenotypically diverse and characterized by a severe, nonprogressive, inherited reduction in night vision and rod function. CSNB can have normal or abnormal fundus findings; be autosomal dominant, autosomal recessive, or X-linked in its transmission; and have variable involvement of the cone photoreceptors. Subtypes of CSNB include fundus albipunctatus, Oguchi's disease, flecked retina of Kandori, and familial fleck retina with night blindness. Sometimes reduced visual acuity, myopia, strabismus, or congenital nystagmus may accompany these diseases. Genetic mutations have been identified for several of the different subtypes of CSNB.

Group 2: Inherited Retinal and Choroidal Dystrophies

Several inherited retinal and choroidal dystrophies can cause nyctalopia/night blindness that becomes more symptomatic as the disease progresses. Nyctalopia is usually the initial symptom in retinitis pigmentosa (rod-cone dystrophy). Other inherited ocular diseases with symptoms of nyctalopia include choroideremia and gyrate atrophy.

Group 3: Physiological Aging

Decreased visual function and electrophysiologic responses in the absence of other ocular diseases is a normal part of aging. Factors such as ocular media, pupil size, and physiological changes of the neuronal visual pathway can affect vision, including night vision. Older eyes are also more likely to develop cataracts which may affect vision at night. Full-field electroretinogram (ERG) rod and cone amplitudes have been shown to decline with age, with a more significant decline occurring after age 55 years.

Group 4: Nutritional Factors

Vitamin A deficiency leads to decreased amounts of rhodopsin, an important visual pigment of the rod photoreceptors, with reduced retinal electric activity and resulting nyctalopia/night blindness. Vitamin A deficiency with ocular symptoms of xerophthalmia can be the result of malnutrition with children being more susceptible. Unfortunately this is a major cause of blindness in children in undeveloped countries. Because Vitamin A is a fat-soluble vitamin absorbed in the small intestine and stored in the liver, diseases such as congenital or postsurgical short bowel syndrome, Crohn's disease, liver failure, or alcoholism may also lead to a deficiency.

Group 5: Other Ocular Disorders that Involve Rod Function

Other ocular disorders such as advanced glaucoma and myopia can lead to nyctalopia. Decreased night vision has also been associated with chloroquine toxicity and phenothiazine toxicity.

Clinical Presentation

Presentation of nyctalopia is dependent on the etiology. Patients with congenital hereditary diseases may be unaware of nyctalopia until later in life when they are driving at night. Other patients

may be very sensitive to the fact that they are having more difficulties at night, especially if their disease is progressive.

Visual acuity can range from normal to severely deceased in patients with symptomatic nyctalopia. Clinical exam findings may be normal or may show distinct findings such as bone spicule in the peripheral fundus as seen in retinitis pigmentosa or Bitot's spots on anterior exam seen with Vitamin A deficiency.

Diagnosis

Determining the diagnosis that has led to nyctalopia is helped by a detailed family, medical, and ocular history and complete ocular exam. A targeted work-up can then be conducted. Full-field electroretinograms (ERGs) are helpful in determining photoreceptor functioning. For some inherited diseases such as certain forms of CSNB, retinitis pigmentosa, choroideremia, and gyrate atrophy, genetic testing is available.

Differential Diagnosis

Differential diagnosis of nyctalopia/night blindness should include the potential etiologies discussed above.

Prophylaxis

Genetic counseling exists for families with known inherited ocular diseases. Nutritional causes of nyctalopia can be prevented by monitoring and supplementation in high-risk individuals. Identification of drug retinal toxicities through close monitoring may decrease chances of symptomatic changes.

Patients with hereditary ocular diseases should wear sunglasses in bright light to reduce the likelihood of progression due to oxidative stresses.

Therapy

For inherited causes of nyctalopia, unfortunately no treatments exist. Patients with vitamin A deficiency should be treated with vitamin A supplementation. Stopping drugs with known retinal toxicities may halt or slow retinal changes.

Prognosis

Prognosis is variable dependent on the etiology of the nyctalopia. Nonprogressive, progressive, and reversible forms of nyctalopia exist.

Epidemiology

Epidemiology is very dependent on the cause of nyctalopia and varies between different etiologies.

Cross-References

- ▶ Atypical Retinitis Pigmentosa (RP)
- ▶ Beta Carotene, Use and Dosage of
- ▶ Choroid, Gyrate Atrophy of
- ▶ Choroidal Neovascularization: Myopia
- ▶ Electroretinogram
- ▶ Fundus Albipunctatus
- ▶ Night Blindness
- ▶ Xerophthalmia

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Nystagmus

- ▶ Albinism

Nystagmus: Overview

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Synonyms

None, (although some forms of abnormal eye movements are called "nystagmus" when they are "nystagmoid," microtremor (e.g., superior oblique myokymia), or saccadic intrusions (e.g., opsoclonus or ocular flutter)).

Definition

Nystagmus is a rhythmic oscillation of the eyes that, by definition, has a pathologic slow phase, but it is typically named for the corrective fast-phase jerk component or is termed pendular when there is no fast phase. Although typically bilateral, symmetric, and associated, there are forms that are bilateral but asymmetric, unilateral, or dissociated.

Etiology

Nystagmus can be either physiologic or pathologic. Typically, physiologic nystagmus is of low amplitude, is unsustained, symmetric in both eyes, directed horizontally, and only gaze-evoked in extremes of horizontal gaze (e.g., right beating horizontal jerk nystagmus on right gaze). This is sometimes referred to as "end-position" or "end-gaze" nystagmus. It typically dampens rapidly (i.e., unsustained) and stops when the eyes are brought a few degrees back toward primary. In contrast to most forms of pathologic nystagmus, it is not present in primary position.

Physiologic nystagmus can also be induced by vestibular stimulation (by head rotation or cold or warm water irrigation of the ear) and optokinetic stimulation (by use of the optokinetic drum). Primary position nystagmus is always pathologic and is typically sustained, involuntary, and constant.

Pathologic nystagmus can be further characterized based on the amplitude, vector, direction, and frequency of the nystagmus and is named for the fast phase if present. Additional testing is typically necessary to try to narrow the differential diagnosis based upon morphology of the nystagmus and the response of the nystagmus to various maneuvers (e.g., fixation, gaze, near reaction, occlusion of either eye, head position). Nystagmus can be of central or peripheral origin and is typically localized by "the company it keeps" (see below).

Clinical Presentation

Depending on the etiology, it may be present within several months of birth or acutely after an inciting event. Central and peripheral vestibular nystagmus can often be differentiated by accompanying symptoms and signs. Peripheral nystagmus often occurs in the setting of hearing loss, tinnitus, and positional symptoms and signs.

Diagnostics

Diagnosis of different type of nystagmus is based primarily on clinical exam. A common cause of

nystagmus is medication side effect (especially antiseizure medicines) or toxicity. Unexplained nystagmus should be localized based upon accompanying symptoms and signs. Neuroimaging (preferably magnetic resonance imaging of the brain with and without contrast) is generally required as an initial step in the evaluation of central forms of pathologic nystagmus. Peripheral vestibular nystagmus usually presents to and is managed by otolaryngology (neurootology). Typical laboratory studies depending on the clinical scenario might include vitamin testing (e.g., B12, folate, thiamine), electrolyte testing (e.g., magnesium), inflammatory or autoimmune testing, infectious serology, toxin screen, and neoplastic/paraneoplastic evaluation.

Differential Diagnosis

1. Ocular flutter
2. Opsoclonus
3. Microtremor
4. Voluntary nystagmus

Prophylaxis

Depending on the type of nystagmus, discontinuation of reduction of dose of offending exogenous agents could be considered. There is no prophylaxis for nystagmus and treatment should be directed at the underlying etiology.

Therapy

Complete resolution depends on successful treatment of the underlying etiology, and thus nystagmus may not resolve if the underlying condition is chronic, untreatable, or incurable. Acute demyelinating or inflammatory lesions might respond to corticosteroid treatment. Likewise, compressive lesions might be resectable. Medical treatment for nystagmus has shown unpredictable and variable efficacy and is often empiric. Pharmacologic agents with GABAergic properties such as baclofen have been shown to be successful in treating the acquired form of periodic alternating nystagmus (PAN). Clonazepam occasionally damps downbeat and other central vestibular forms of nystagmus. Other agents that have been used with some success include memantine or gabapentin. Nonmedical treatments include base-out prisms, and contact lenses may improve visual acuity in congenital nystagmus and damping the nystagmus. Surgical treatment with Anderson-Kestenbaum procedure can mechanically shift the null point (if present) to primary position and correct anomalous head positions in patients with congenital or acquired nystagmus.

Prognosis

Prognosis is dependent on the underlying etiology.

Epidemiology

The prevalence of nystagmus in the general population was estimated to be 24.0 per 10,000 population in one study.

See Table 1 for different types of nystagmus.

Other topics related to nystagmus.

Heading

Oculopalatal myoclonus (OPM)

Definition

OPM is a form of acquired pendular nystagmus characterized by rhythmic conjugate eye movements in the vertical plane.

Etiology

It can be seen in patients with multiple sclerosis but can occur after any lesion (e.g., hemorrhage, tumor, trauma) in the Guillain-Mollaret triangle (see below).

Nystagmus: Overview, Table 1 Different forms of nystagmus

Heading	Peripheral vestibular nystagmus (PVN)	Seesaw nystagmus (SSN)	Upbeat nystagmus	Periodic alternating nystagmus	Congenital nystagmus	Downbeat nystagmus (DBN)
Definition	Typically related to acute or chronic vestibular neuropathy	SSN is a central form of vestibular nystagmus. It is a combination of vertical and torsional components. It is characterized by disconjugate, alternating depression and extorsion of one eye with concomitant elevation and intorsion of the fellow eye. The oscillations are typically pendular (sinusoidal, with both phases having equal velocity), but can be jerk (slow-phase drift followed by fast-phase correction)	Upbeat nystagmus is often found in patients with lesions in the posterior fossa (most commonly in the medulla or, to a lesser degree, the anterior cerebellar vermis)	A type of central vestibular nystagmus characterized by purely horizontal component that reliably changes direction approximately every 1–2 min	May occur with congenital strabismus	DBN is a type of central vestibular nystagmus characterized by involuntary, slow upward drifting of the eyes immediately followed by a fast, downward saccade. It also obeys Alexander's law in that the DBN increases in downgaze
	Characterized by a combination of horizontal and torsional components			Acquired forms are typically caused by insults to the cerebellar nodulus and uvula, which play an important role in the time constant of rotational velocity storage	Congenital nystagmus is a conjugate horizontal nystagmus that demonstrates increased slow-phase velocity with distant fixation and diminishment by convergence. The horizontal direction of the nystagmus remains horizontal even in up- and downgaze. The movements can be jerk and/or pendular pattern	
	The slow phase is toward the side of the lesion with a corrective saccade away from the side of the lesion. It follows Alexander's law					
Etiologies	Dysfunction of the inner ear labyrinth or vestibular nerve (e.g., benign paroxysmal positional vertigo (BPPV), labyrinthitis, Meniere's disease, trauma, and central etiologies (e.g., cerebellopontine angle tumors), which provides sensory information regarding balance and spatial orientation to the brain. Without normal	SSN may be congenital or acquired but is most commonly found with structural lesions in the parasellar and third ventricular region (especially craniopharyngioma). Other etiologies for SSN include stroke, trauma, congenital Chiari malformation, or demyelinating disease	Common etiologies include tumor, demyelination, stroke, cerebellar degeneration, or tobacco smoking	PAN can be congenital or acquired. In acquired forms, common etiologies include demyelination, stroke, cerebellar degeneration, Chiari type 1, anticonvulsant therapy, or bilateral vision loss	It may be hereditary, genetic (associated with oculocutaneous albinism and aniridia), or spontaneous	Disruption in the neuronal transmission between vestibulocerebellum, the anterior semicircular canals, and the ocular motoneurons usually results in DBN. It may be congenital or acquired and often due to structural lesions at the cervicomedullary junction (most commonly Chiari type 1 malformation). Other

	vestibular afferent inputs, the eye cannot be stabilized in eccentric locations					etiologies for DBN include drugs (e.g., codeine, alcohol, lithium, anticonvulsants), tumors, nutritional problems (e.g., Wernicke syndrome, magnesium deficiency), paraneoplastic syndromes, demyelination, and stroke
Clinical presentation	PVN is usually acute in onset and often associated with marked disequilibrium characterized by vertigo, nausea, vomiting, and tinnitus. Patients may also have oscillopsia and hearing loss. The symptoms are often made worse by particular head postures or head movements	SSN has an obvious and dramatic morphology that makes the diagnosis clinically. Patients often have concomitant visual loss or a bitemporal hemianopsia localizing to the chiasm	Patient usually presents acutely with nystagmus that increases in amplitude with upgaze	The cycle begins with a jerk phase in one direction, with its amplitude and frequency progressively increasing and then decreasing until the nystagmus stops for a period of seconds. Subsequently, the jerk phase begins in the opposite direction following the same crescendo-decrescendo pattern until the nystagmus stops briefly again; then, the cycle repeats itself. Acquired form of PAN has an oscillation cycle of 2–4 min.	Congenital nystagmus is usually acute in onset and develops within the first 6 months of life. Visual acuity may be decreased (probably by the nystagmus itself and seldom below a level of 20/200), but can be normal (especially at near, where convergence effort might dampen the nystagmus and improve near acuity). Unlike patients with acquired nystagmus, patients with congenital nystagmus do not experience oscillopsia (the sensation that the environment is moving). Many cases have superimposed latent component, and the patient might have an anomalous head position to achieve a null point where the nystagmus is least	DBN may be congenital or acquired and is often associated with good vision and normal neurologic findings. If it is the hereditary or degenerative forms, the DBN may precede the clinical or radiographic findings of the spinocerebellar degeneration. More often, it is of acute onset secondary to a structural lesion

(*continued*)

Nystagmus: Overview, Table 1 (continued)

Heading	Peripheral vestibular nystagmus (PVN)	Seesaw nystagmus (SSN)	Upbeat nystagmus	Periodic alternating nystagmus	Congenital nystagmus	Downbeat nystagmus (DBN)
Diagnostic	Diagnosis of PVN is based primarily on clinical exam. A typical feature of PVN that helps distinguish it from central causes of nystagmus is suppression of nystagmus with visual fixation. Many different modalities can be used to elicit this response, including Frenzel's glasses, video-oculography, or simply using direct ophthalmoscopy and intermittently covering the fellow eye during viewing. The Dix-Hallpike maneuver might identify a patient with BPPV	Diagnosis of SSN is based primarily on clinical exam. Visual field testing and a full neuro-ophthalmologic examination are indicated	Diagnosis of upbeat nystagmus is based primarily on clinical exam	Diagnosis is based primarily on clinical exam. It is important when evaluating a patient with horizontal nystagmus to watch the patient's eyes for at least 2 min to ensure that PAN is not the cause of the horizontal nystagmus	Diagnosis is based primarily on clinical exam. Two unique features of congenital nystagmus are inversion of optokinetic response and damping of nystagmus with convergence and eyelid closure	Diagnosis of DBN is based primarily on clinical exam
Differential diagnosis	1. Central vestibular nystagmus	1. Downbeat nystagmus	1. Downbeat nystagmus	1. Congenital nystagmus	1. PVN	1. Upbeat nystagmus
	2. Bruns nystagmus	2. Upbeat nystagmus	2. Seesaw nystagmus	2. Seesaw nystagmus	2. Periodic alternating nystagmus (PAN)	2.
				3. Internuclear ophthalmoplegia	3. Internuclear ophthalmoplegia (INO)	2. Seesaw nystagmus
					4. Congenital sensory nystagmus (characterized by a complex searching nystagmus consisting of irregular pendular (sinusoidal) and jerk features secondary to abnormalities of the eyes or optic nerves, present at birth or acquired in childhood)	3. Oculopalatal myoclonus

Therapy	The treatment of PVN acutely is typically supportive, but there are also medications such as meclizine or scopolamine to decrease vertigo symptoms. Vestibular exercise programs and rehabilitation are helpful in many patients. If the diagnosis is BPPV, then repositioning maneuvers can be performed by the ENT specialist	Definitive treatment of SSN depends upon treating the underlying etiology; however, medications such as baclofen, gabapentin, and clonazepam may help to abate the nystagmus	Definitive treatment depends upon the etiology; however, medications such as baclofen, gabapentin, and clonazepam may help to abate the nystagmus	Treatment is depending on the etiology. Acquired form of PAN also responds well to baclofen, which is the first-line therapy for PAN. Gabapentin, clonazepam, and memantine have also been used in PAN anecdotally and in other forms of acquired nystagmus with variable results	Nonmedical treatments include base-out prisms, and contact lenses may improve visual acuity in congenital nystagmus and damping the nystagmus	Treatment is depending on the etiology. If the MRI shows a symptomatic Chiari malformation, then decompression of the area may result in complete resolution of DBN. Other pharmacologic treatment options include 4-aminopyridine, gabapentin, benzodiazepines, memantine, and baclofen. Base-out prisms may also be employed to stimulate fusional convergence and improve visual acuity, which damps the nystagmus. A null point may be present and surgically or medically treated
Prognosis	Depending upon the etiology, PVN symptoms may spontaneously resolve over a few days to weeks; however, resolution may be incomplete requiring further evaluation and treatment by ENT. Even then, patients may experience discomfort with activities that challenge their vestibular system	Prognosis is depending upon the etiology of SSN	Prognosis depends on the etiology of the nystagmus	Prognosis depends on the etiology of the nystagmus	About 15% of congenital nystagmus patients also have congenital strabismus and of which congenital esotropia is the most common type. To utilize a null point, some of these children will adopt a preferred gaze position, and the anomalous head position may become more obvious as the child reaches school age. Surgical or prism therapy might be useful to move the null point to primary position	Prognosis depends on the etiology of the nystagmus

(*continued*)

Nystagmus: Overview, Table 1 (continued)

Heading	Peripheral vestibular nystagmus (PVN)	Seesaw nystagmus (SSN)	Upbeat nystagmus	Periodic alternating nystagmus	Congenital nystagmus	Downbeat nystagmus (DBN)
Epidemiology	BPPV is the most common form of positional vertigo, accounting for nearly one-half of patients with PVN. It represents up to 18% of patients seen in dizziness clinics, and 25% of patients referred for vestibular testing end up with a diagnosis of BPPV. In one population-based survey study, the lifetime prevalence of BPPV was 2.4% with increased frequency with increased age (up to seven times higher in those older than age 60 years), and BPPV is more common in women	SSN can affect any age and either gender	Can affect any age, any patient, and either gender depending on the underlying etiology	Can be congenital or acquired and can affect any age patient, any race, and either gender	CN usually develops within the first 6 months of life and thus is not typically present at birth	
Cross-references	1. Benign paroxysmal positional vertigo	1. Chiari malformation	Alexander's law	Chiari type 1	1. Congenital sensory nystagmus	1. Upbeat nystagmus
	2. Alexander's law	2. Pituitary adenoma			2. Nystagmus blockage syndrome	2. Seesaw nystagmus
	3. Meniere's disease	3. Craniopharyngioma				3. Oculopalatal myoclonus
	4. Cerebellopontine angle					

Clinical Presentation

OPM typically presents with a delayed manifestation that appears months to years after damage to the brainstem (often pontomedullary infarct or hemorrhage) within the Guillain-Mollaret triangle. This anatomic triangle includes pathways between the red nucleus, ipsilateral inferior olivary nucleus, and contralateral dentate nucleus. Patients often complain of severe oscillopsia due to the high-amplitude, vertical, pendular nystagmus. It may be associated with synchronous contractions of the palate, face, pharynx, and other muscle groups.

Diagnostic

In any patient with a vertical, pendular nystagmus (i.e., not clearly upbeat or downbeat nystagmus (DBN)), the key and differentiating feature of oculopalatal myoclonus can be demonstrated by having the patient open their mouth for the clinician to observe the palate (uvula) for abnormal vertical movements. The palatal myoclonus can also occur independent of the eye findings. The typical MRI findings include the primary inciting lesion in the Guillain-Mollaret triangle, and there may be hyperintensity and hypertrophy of the inferior olivary nucleus on T2-weighted images in the medulla.

Differential Diagnosis

1. Torsional nystagmus
2. Downbeat nystagmus
3. Internuclear ophthalmoplegia
4. Congenital pendular nystagmus

Heading

Internuclear ophthalmoplegia

Definition

It is a disconjugate eye movement characterized by a non-sustained, dissociated horizontal abducting nystagmus in the eye contralateral to the medial longitudinal fasciculus (MLF) lesion during lateral gaze away from the side of the lesion. There is also a concomitant slowing, paresis, or absence of adduction in the eye ipsilateral to the lesion.

Etiology

The medial longitudinal fasciculus (MLF) coordinates conjugate eye movements. Lesions to the MLF result in disconjugate movement called internuclear ophthalmoplegia (INO). Common lesions to the MLF are most commonly caused by demyelinating disease, but cerebrovascular accidents or brain tumors may also occur. The INO may be unilateral or bilateral, but bilateral INO in a young patient is typically demyelinating disease.

Clinical Presentation

Typically acute in onset. Patient often complains of double vision.

Diagnostic

Diagnosis of an INO is based primarily on clinical exam. In patients with INO, the eye ipsilateral to the lesion adducts slowly or not at all, and the abducting eye shows a characteristic horizontal nystagmus on contralateral gaze. Upon convergence, both eyes adduct normally (including the eye ipsilateral to the lesion). Skew deviation may be present in addition to exotropia.

Differential Diagnosis

1. Peripheral vestibular nystagmus (PVN)
2. Periodic alternating nystagmus (PAN)

Heading

Opsoclonus

Definition

"Dancing eyes and dancing feet (myoclonus)."

Opsoclonus is a bilateral saccadic intrusion abnormality that is characterized by involuntary, fast (saccadic), multidirectional, conjugate ocular movements. It is not technically a form of nystagmus because it lacks a slow-phase movement. It is considered a more severe form of ocular flutter (which is similar in morphology except that in contrast to the multivectorial opsoclonus, ocular flutter only occurs in the horizontal plane).

Etiology

In adults, the most common etiologies for opsoclonus are postinfectious and paraneoplastic. In children, however, paraneoplastic opsoclonus due to neuroblastoma may be present in up to 50% of cases.

Clinical Presentation

Opsoclonus is usually acute in onset and often associated with markedly rapid, high-frequency, and low-amplitude ocular oscillation.

Diagnostic

Diagnosis of opsoclonus is based primarily on clinical exam. Other nonneoplastic lesions in the brainstem can also produce the finding however (e.g., inflammatory, infectious, traumatic, demyelinating, metabolic, toxic, etc.).

Differential Diagnosis

Infantile nystagmus

Therapy

Opsoclonus in children or adults should prompt a neoplastic and paraneoplastic workup, as approximately 20% of adults with opsoclonus have an underlying malignancy (typically neuroblastoma, small cell lung carcinoma, breast cancer, or ovarian cancer).

Treatment is depending on the etiology. If neuroblastoma is present, surgical removal of the tumor is recommended. Because the mechanism of opsoclonus in neuroblastoma patients is hypothesized to be paraneoplastic, additional treatment includes intravenous corticosteroids, immunoglobulin, or rituximab.

Cross-References

► Flutter, Ocular

Further Reading

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O

Occipital Lobe Lesion

► Retrochiasmal Disorders

Occipital Seizures: Transient Visual Loss

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Definition

Occipital lobe epilepsy (OLE) refers to recurring seizures that originate in the occipital lobe of the brain. OLE is an uncommon form of epilepsy, and patients with this condition may experience a multitude of visual disturbances immediately before, during, and after a seizure has occurred.

Etiology

While the exact etiology is unknown, possible predisposing findings include underlying tumors, vascular malformations, developmental abnormalities, or other pathology in the occipital lobe.

Clinical

Visual auras such as unformed images, flashes, steady white or colored lights, and very complex visual hallucinations are common in patients with occipital lobe seizures. The occipital seizure visual phenomena are often described as geometric, colored figured (especially small circles). Other reported visual distortions include macropsia and micropsia (change in size), metamorphopsia (change in shape), and dyschromatopsia (change in color). The visual aura usually manifests in the contralateral visual field, but bilateral and diffuse symptoms may also occur. These seizures often start in and can remain localized to the occipital lobe but can also spread to affect other areas of the brain.

In the ictal state, patients with OLE may present with bilateral simultaneous transient vision

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loss, which can extend into the post ictal state that might include incoherence or mental status change. The duration of the vision loss can range from less than 1 min to days, or it can become more constant. Loss of consciousness and progression to more severe generalized seizures with bilateral motor convulsions depends on each individual patient and the extent of central nervous system (CNS) spread of the initial focal seizure. Finally, occipital seizures in children may be benign occipital epilepsy of childhood. Spontaneous remission in these patients usually occurs by 12 or 13 years of age but some patients have persistent OLE.

Differential Diagnosis

The differential diagnosis of OLE is similar to that of any seizure disorder. Other conditions to consider include migraine, sleep disorders, medication side effects, and psychiatric conditions.

Diagnosis

Diagnosis typically includes history, electroencephalogram (EEG), and magnetic resonance imaging of the brain.

Treatment

Treatment for OLE typically includes anticonvulsants like carbamazepine. The use of these medications can improve the vision of patients suffering from vision loss, as well as to help prevent occurrence of future generalized seizures.

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Ocular Allergies

► Allergic Conjunctivitis

Ocular Bobbing

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Synonyms

Atypical bobbing; Monocular bobbing

Definition

Ocular bobbing is a type of spontaneous abnormal eye movement that presents as a rapid downward

movement of both eyes followed by a slow drift back into primary position (Lavin 2012). The oscillation typically recurs at irregular intervals between 2 and 15 times per minute (Lavin 2012).

Etiology

Ocular bobbing occurs in patients that are usually comatose or in a stupor due to severe damage to the pons or less commonly a diffuse encephalopathy of toxic or metabolic orgin (Quiros and Yee 2014). In these situations, the brainstem is relatively intact and the bilateral lesions are above the brainstem (Berger 2012). Damage to the pons can occur in severe central pontine ischemic destruction, central pontine myelinolysis, encephalitis, or extra-axial pontine compression (e.g., cerebellar tumor or hematoma) (Quiros and Yee 2014). Toxicity (e.g., organophosphate poisoning) can also ocular bobbing. Although typical ocular bobbing is highly specific for acute pontine lesions, the finding is not pathognomonic.

Classifications

The typical form is associated with paralysis of both reflex and spontaneous horizontal eye movements. Monocular or paretic bobbing occurs when a coexisting ocular motor palsy alters the appearance of typical bilateral ocular bobbing. Atypical bobbing refers to all other variations of bobbing that cannot be explained by ocular palsy superimposed on typical bobbing (Berger 2012).

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Ocular Chrysiasis

▶ Chrysiasis, Corneal Pigmentation

Ocular Cicatricial Pemphigoid (OCP)

▶ Pemphigoid, Cicatricial

Ocular Hypopigmentation

▶ Albinism

Ocular Hypotony

▶ Hypotony

Ocular Lice

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Synonyms

Eyelash pediculosis; *Pediculosis ciliaris*; *Pediculosis palpebrarum*

Definition

Lice infestation of the eyelashes and/or eyebrows caused by *phthirus pubis*.

Etiology

Phthirus pubis is a hematophagous parasite. *Phthirus* measure up to 2 mm in length and have a broad, crab-like body that distinguishes them from the longer and more slender *pediculosis palpebrarum*, or head louse. *Phthirus* are usually transferred by hand contact from genital areas to the eye but can also be transmitted interpersonally through direct contact (e.g., linens, clothing) (Anderson and Chaney 2009).

Clinical Presentation

Patients present with complaints of itching, crusting, and irritation of eyelid margins. Conjunctival inflammation, usually bilateral, is often present (Barreto et al. 2012). A history of close personal contacts with similar symptoms is often elucidated.

Diagnosis

Visualization of affected eyelashes and eyebrow hair through the slit lamp will uncover the parasites. Translucent eggs (nits) measuring around 0.5 mm can be visualized in the eyelashes. Accumulation of reddish-brown granular fecal material at the base of lashes may assist with diagnosis if the translucent parasite is difficult to see. A follicular conjunctivitis is often seen.

Differential Diagnosis

Allergic contact dermatitis, blepharitis, blepharoconjunctivitis, bacterial or follicular conjunctivitis, eyelid eczema, and ocular rosacea (Turgut et al. 2009).

Prophylaxis

Sexual partners and very close family members can be treated prophylactically as outlined below to prevent cross reinfection. Bedding and perhaps furniture, which is shared by the patient with others, should be thoroughly cleaned at a temperature greater than 130 °F.

Therapy

Mechanical removal of lice and nits using fine tweezers and twice-daily application of petroleum jelly or other ophthalmic ointment to the eyelashes and eyebrows for at least 1 week should be initiated to suffocate the organisms (Chapel et al. 1979). Successful management has been reported with oral ivermectin (two doses of 200 mcg/kg PO 1 week apart), pilocarpine 4% gel drops, 1% yellow oxide of mercury ointment, permethrin 1% cream, malathion 1% shampoo, and lindane 1% lotion (Couch et al. 1982). Other areas of body hair should be treated with gamma benzene hexachloride shampoo. The occurrence of lice in preadolescents may indicate sexual abuse and appropriate investigation should be considered.

Prognosis

Excellent, provided course of treatment is followed. Nits can remain dormant for 7–10 days so eradication of only visible lice is insufficient.

Epidemiology

The exact incidence is unknown, but ranges between 1% and 2% occurrence worldwide among adults is generally reported.

Cross-References

- ▶ Blepharitis
- ▶ Blepharoconjunctivitis
- ▶ Eczema, of Eyelid

► Follicular Conjunctivitis
► Rosacea: Overview

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Ocular Medication Absorption Affected by Viscosity

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Definition

Viscosity is one of the several drug vehicle characteristics that can affect the amount of time a drug stays on the cornea, the penetration rate into the cornea, and its bioavailability. All else being constant, the more viscous the ocular drug the longer it stays on the cornea and the better its bioavailability.

Cross-References

► Capsule-Type Drug Delivery System

Ocular Melanoma

► Uveal Melanoma

Ocular Melanosis

► Blue Nevus

Ocular Migraine

► Retinal/Ocular Migraine

Ocular Motor Apraxia

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Synonyms

Voluntary gaze paresis

Definition

Ocular motor apraxia is defined as a deficit in the voluntary control of purposeful conjugate eye movements without lesion in the extraocular muscles, neuromuscular junction, or ocular motor nerve pathways for eye movements. Children with this condition have difficulty moving their eyes horizontally.

Etiology

The etiology of ocular motor apraxia (OMA) can be congenital or acquired. Congenital ocular motor apraxia (COMA) has been hypothesized to be due to abnormality of the vermis of the cerebellum. Acquired ocular motor apraxia can occur from bilateral lesions of the parieto-occipital region, which controls voluntary visual saccades and pursuit, ataxia-telangiectasia, inherited spinocerebellar ataxia, Joubert syndrome, Gaucher disease, Niemann-Pick disease, Balint syndrome, and rarely following cardiac surgery.

Clinical Presentation

COMA patients present with the characteristic head thrust movement (using the vestibular ocular reflex (VOR)) to compensate for the voluntary deficiency of conjugate eye movement. Some cases of OMA occur in association with perinatal hypoxia, post-infection (e.g., meningitis, encephalitis, sepsis), periventricular leukomalacia, cerebral palsy, and seizure disorders.

Diagnostics

Patients with the supranuclear ocular motor apraxia can be diagnosed clinically by overcoming the deficit with the dolls head maneuver (using VOR). In COMA cases patients may also demonstrate the characteristic head thrust movement.

Differential Diagnosis

- Progressive supranuclear palsy
- Ocular motor palsy, nonorganic

Therapy

There is no therapy for congenital ocular motor apraxia.

Prognosis

Prognosis depends on the etiology. The head thrusts in COMA often diminish over time but may not completely resolve.

Epidemiology

COMA is congenital, but acquired OMA may affect patients of any age, either gender, and any ethnic group.

Cross-References

► Congenital Ocular Motor Apraxia
► Oculomotor Nerve Palsy

Further Reading

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Ocular Pressure Patch

► Corneal Patching

Ocular Prostheses

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Synonyms

Prosthesis; Scleral shell (to be used only when it covers an eyeball which may be blind, unsightly, and/or phthisical)

Definition

A prosthetic that is designed to fit within the eye socket. Iris, pupil, scleral tint, and vascular pattern are usually hand duplicated in detail to match the fellow eye. A prosthetic can be fitted in a socket that has undergone enucleation or evisceration; it can also be fitted over a disfiguring, blind, or phthisical eye (referred to as a scleral cover shell). Today, most prosthetic eyes are acrylic based; however, glass is still used in certain parts of the world (2008).

Indications

1. Provides an optimal cosmetic appearance and some variable motility after undergoing enucleation or evisceration
2. Covers a disfiguring phthisical eye that is still retained in the socket (scleral cover shell)
3. Provides orbital bone growth in cases of congenital anophthalmos and microphthalmos
4. Prevents contractures from occurring in a socket that has undergone trauma, chemical burn, radiation therapy, or infection

Techniques and Principles

Once the socket is deemed in satisfactory postoperative condition by the surgeon after undergoing enucleation or evisceration, the patient will visit an ocularist for the prosthetic fabrication. Impressions of the socket are made, and the impression is then translated into the creation of an individualized prosthetic. In cases of a blind or phthisical eye, they can be referred to an ocularist once they are free from any active ocular issues (i.e., pain, infection) (Stewart 1995).

Management and Care

The average life of a prosthesis is 4–6 years, but varies widely. Proper polishing should be done by an ocularist approximately once a year. Removal of the prosthetic and evaluation of the socket cavity is essential in an ophthalmologic exam. Chronic irritation and excessive mucous discharge most commonly result from improperly fitted prosthetic, lower lid malposition, or abnormal surface condition of the prosthetic.

Cross-References

- ▶ Enucleation
- ▶ Evisceration
- ▶ Contracted Socket

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Ocular Siderosis

- ▶ Siderosis: Signs and Symptoms

Ocular Surface Staining

► Exposure Staining, Keratoconjunctivitis Sicca

Oculo-Auriculo-Vertebral Spectrum

► Goldenhar Syndrome

Oculocephalic Reflex

► Doll's Head Maneuver/Phenomenon, in Horizontal Gaze Palsy

Oculocraniosomatic Disorder

► Kearns Syndrome

Oculocraniosomatic Neuromuscular Disorder with Ragged Red Fibers

► Kearns Syndrome

Oculodentodigital (ODD) Syndrome

► Oculodentoosseous Dysplasia

Oculodentoosseous Dysplasia

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Synonyms

Oculodentoosseous dysplasia is more commonly known as oculodentodigital dysplasia. Other synonyms include:

Oculodentodigital (ODD) syndrome; ODD dysplasia (ODDD)

Definition

Oculodentodigital dysplasia (ODDD) is a rare genetic disorder leading to a congenital ectodermal dysplasia, which manifests as developmental abnormalities of the face, eyes, limbs, and teeth (Duke-Elder 1972).

Etiology

ODDD is an autosomal dominant condition resulting from a mutation of the gap junction alpha 1 (GJA1) gene encoding for connexin 43 (Paznekas et al. 2003). There have been reports of an autosomal recessive variant (Frasson et al. 2004).

Clinical Presentation

Patients may present with decrease vision resulting from glaucoma, the most common cause of vision loss in ODDD (Traboulsi and Parks 1990). If there is suspicion for ODDD, family members should be examined to look for signs consistent with ODDD. Patients with glaucoma may present as early as infancy, those without, may never be diagnosed.

Characteristic findings include:

- Nasal abnormalities
  - Narrow nose
  - Hypoplastic alae nasi
  - Small anteverted nostrils
  - Prominent columnella and nasal bridge
- Brittle nails
- Hypotrichosis
- Teeth abnormalities
  - Hypodontia
  - Microdontia
  - Enamel hypoplasia
  - Dental carries
- Digital abnormalities
  - Syndactyly (bilateral of fourth and fifth digits)
  - Clinodactyly

- Ocular abnormalities
  Microcornea
  Microphthalmia
  Reduced palpebral fissure length
  Iris abnormalities
  Cataracts
  Glaucoma (congenital, juvenile, angle closure, and primary open angle)
  Foveal hypoplasia
  Optic nerve head dysplasia
- Neurologic symptoms

Autosomal recessive forms have exhibited intracranial calcifications, hearing loss, and persistent hyperplastic vitreous (Duke-Elder 1972; Frasson et al. 2004; Musa et al. 2009; Gabriel et al. 2011).

Diagnosis

Diagnosis is based on the presence of clinical findings consistent with ODDD and/or the presence of a GJA1 mutation.

Differential Diagnosis

Hallermann-Streiff syndrome, Mohr-Clausen syndrome (oro-facial-digital syndrome type II), keratitis-ichthyosis-deafness (syndrome), ectrodactyly-ectodermal dysplasia-cleft syndrome, congenital glaucoma, juvenile glaucoma.

Prophylaxis

Regular screening for ophthalmic complications, most notably glaucoma, is warranted in a person with ODDD. If a person has ODDD, a discussion with a genetic counselor may assist in the decision process with regard to having children.

Therapy

Therapy is aimed at managing complications of ODDD. Glaucoma is managed depending on the cause (congenital, open angle, or angle closure) (Traboulsi and Parks 1990). Patients should have regular dental examination due to their increased risk for dental carries.

Prognosis

The prognosis is good. Most cases do not have cognitive impairment. The autosomal recessive variant may be more severe and have a poorer prognosis.

Epidemiology

The incidence of ODDD is unknown. It is present equally in males and females and has been reported primarily in white race/ethnicity.

Cross-References

- ▶ Angle Closure
- ▶ Angle-Closure Glaucoma
- ▶ Primary Congenital Glaucoma
- ▶ Microcornea
- ▶ Microphthalmos (Microphthalmia)
- ▶ Pediatric Glaucoma

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Oculoglandular Syndrome

► Oculoglandular Syndrome, Parinaud

Oculoglandular Syndrome, Parinaud

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Synonyms

Oculoglandular syndrome

Definition

Parinaud's oculoglandular syndrome is the combination of granulomatous conjunctivitis in one eye and ipsilateral preauricular or cervical adenopathy.

Etiology

The most common cause is cat-scratch disease (CSD, *Bartonella henselae*). Other frequent causes are tularemia (*Francisella tularensis*) and sporotrichosis (*Sporotrichum schenckii*). Occasional causes include tuberculosis (*Mycobacterium tuberculosis*), syphilis (*Treponema pallidum*), and coccidioidomycosis (*Coccidioides immitis*). Viruses, fungi, and parasites are also possible causes. The organism may gain entry to the eye through the conjunctiva or from scratches (Krachmer et al. 2011).

Clinical Presentation

The presentation of Parinaud's oculoglandular syndrome differs depending on the etiology. In oculoglandular CSD, conjunctival lesions measuring 3–4 mm in diameter anywhere in the palpebral or bulbar conjunctiva appear within 1–3 weeks. Conjunctival nodules can be red, white, yellow, or gray and may be inflamed. Eyelid swelling is mild, and conjunctival ulceration may occur over the underlying granuloma. Enlarged preauricular, cervical, or submaxillary lymph nodes accompany the conjunctival granulomas. Other causes (e.g., tularemia, tuberculosis) can present with conjunctival ulceration. Symptoms include a red, irritated, painful eye, possibly fever, and a general ill feeling (Tu 2012).

Diagnosis

Patient history should include contact with pets and wild animals, with subsequent workup of serum and conjunctival cultures. Physical examination may show a red, tender, inflamed eye, tender preauricular lymph nodes, and/or conjunctival nodules. A fourfold increase in immunofluorescent antibody (IFA) serum titers and sometimes PCR-based techniques are useful in identifying *Bartonella henselae* and many other bacteria. The diagnosis of CSD is based on the following: (1) lymphadenopathy, (2) history of cat contact or recent cat scratch or bite, (3) presence of primary inoculation site, (4) positive IFA or PCR test for *B. henselae*, and (5) absence of other causes of lymphadenopathy.

Differential Diagnosis

Cat-scratch disease, tularemia, sporotrichosis, tuberculosis, syphilis, coccidioidomycosis, many rare bacterial causes (e.g., sarcoidosis, chancroid, lymphogranuloma venereum, etc.), virus/fungus/parasite.

Prophylaxis

Frequent hand washing after handling pets, avoid being scratched by cats, avoid contact with wild animals.

Therapy

Depending on the cause of the infection, appropriate antibiotics can be used, especially in immunocompromised patients. Rarely, surgery may be necessary to clear infected tissue.

Prognosis

CSD and its oculoglandular complications are usually self-limited in immunocompetent patients. In immunocompromised patients, CSD is more aggressive and can progress to disseminated infection. If diagnosis and treatment occur early, outcomes are generally very good.

Epidemiology

Parinaud's oculoglandular syndrome is generally a rare presentation, e.g., CSD (4–8%) and tularemia (1%).

Cross-References

► Cat Scratch Disease
► Conjunctivitis

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Oculomandibulofacial Dyscephaly

► Oculomandibulofacial Dyscephaly (Hallermann-Streiff Syndrome)

Oculomandibulofacial Dyscephaly (Hallermann-Streiff Syndrome)

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Synonyms

Francois dyscephalic syndrome; Oculomandibulofacial dyscephaly

Definition

Hallermann-Streiff syndrome (HSS) is clinically defined by its characteristic skull morphology, brachycephaly with frontal bossing, microphthalmia, cataracts, hypotrichosis, micrognathia, beaked nose, dental abnormalities, atrophy of skin, and short stature. The clinical diagnosis is felt to be especially doubtful in the absence of microphthalmia or cataracts.

Etiology

HSS is of rare sporadic inheritance.

Clinical Presentation

Patients typically present at a young age with skeletal and craniofacial abnormalities; poor vision; skin atrophy, especially in the facial regions; and alopecia along suture lines, along with ocular abnormalities. Clouding of the lenses may be seen at birth. Given the association with tracheomalacia, patients may also present with snoring or daytime hypersomnolence. Clinicians should recognize that these patients pose a difficult airway if general anesthesia and intubation are to be attempted.

Additional ophthalmologic manifestations as catalogued by Roulez and colleagues in 2008

include blue sclera, antimongoloid slanting of the palpebral fissures, keratoglobus, iris atrophy, peripheral anterior synechiae, posterior synechiae, persistent fetal vasculature, amorphous retrolenticular membrane, vitreous opacities, optic disc pallor, optic nerve coloboma, chorioretinal pigmentary changes, retinal folds, and glaucoma. The glaucoma in HSS is felt to be of phacolytic etiology from progression of cataract.

Diagnosis

There is no available laboratory diagnosis.

Differential Diagnosis

Hutchinson-Gilford progeria, Werner syndrome, oculodentodigital dysplasia, acromandibular dysplasia, lethal osteocraniostenosis.

Prophylaxis

There is no prophylaxis for this systemic congenital disorder.

Therapy

Early ophthalmologic evaluation in patients with HSS and surgical removal of the congenital cataracts are recommended to optimize visual prognosis. Evaluation should include ultrasound biometry to assess axial length, given the presence of microphthalmia or nanophthalmos. Optical coherence tomography and electroretinography have also been used in isolated cases where HSS patients also had retinal pigmentary changes. Consultation with craniofacial and ear, nose, and throat specialists is recommended to address dental and airway issues, respectively. Patients should receive counseling on the importance of dental hygiene, and surgical correction of clinically significant malocclusion has been recommended, which may also address respiratory issues related to micrognathia.

Prognosis

Patients may experience poor vision and amblyopia if cataract extraction is not performed at an early age. Vision potential is difficult to ascertain given the sporadic nature of the syndrome. The role of corneal opacities and retinal pigmentary changes on final visual outcome has not been definitely ascertained. Feeding difficulties and obstructive sleep apnea should also be recognized and evaluated. Given the sporadic nature of HSS, there is insufficient data on long-term functional outcomes in these patients.

Epidemiology

The disease is of sporadic inheritance, and about 150 cases have been reported globally since its first description in 1893.

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Oculomotor Nerve

► Cranial Nerve III (Oculomotor Nerve)

Oculomotor Nerve Palsy

► Third Nerve Palsy

Oculosympathetic Paresis

► Anisocoria of Small Pupil: Horner Syndrome
► Anisocoria of the Small Pupil

Ocusert Delivery System

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Synonyms

Capsule-type drug delivery system

Definition

The ocusert delivery system consists of a drug reservoir surrounded by two thin drug release-controlling membranes, made of ethylene vinyl acetate (EVA) copolymer. This system is held together by a retaining EVA ring. The drug is delivered by dissolving in the EVA and diffusing along a concentration gradient. It is delivered to the eye at a constant rate (zero-order kinetics) for a given time interval.

This is the first rate-controlled and rate-specified drug delivery system and therefore improves the selectivity of the drug's action.

Cross-References

► Capsule-Type Drug Delivery System

ODD Dysplasia (ODDD)

► Oculodentoosseous Dysplasia

Off-Center Optics

► Decentration

Oncilon-A

► Intravitreal Triamcinolone

Oncocyte

► Oncocytoma

Oncocytoma

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Synonyms

Nodular oncocytosis; Oncocyte; Oxyphile cell adenoma; Oxyphilic cystadenoma

Definition

Oncocytomas are benign proliferations of cells that arise from the epithelium of glandular tissue and are chiefly located in the head and neck region (Biggs and Font 1977; Eglen 1982; Morgan et al. 1998; Mete and Asa 2010; Say et al. 2012). While these adenomas have been reported to occur in the salivary gland, thyroid, parathyroid, pituitary,

kidney, breast, and gastrointestinal tract (Biggs and Font 1977; Eglen 1982; Morgan et al. 1998; Mete and Asa 2010; Say et al. 2012), this article will focus on oncocytomas arising in the ocular adnexa. The majority of ocular oncocytic lesions are located in the caruncle, but they have also been reported to arise in the conjunctiva, eyelid, lacrimal sac, lacrimal gland, and plica semilunaris (Biggs and Font 1977; Eglen 1982; Say et al. 2012). Malignant oncocytic adenocarcinomas have been reported in the literature, but they are exceedingly uncommon (Biggs and Font 1977; Eglen 1982; Morgan et al. 1998; Say et al. 2012).

Etiology

The etiology of oncocytomas is not completely understood, but recent evidence suggests that the formation of these lesions may be related to mutations in the genes affecting oxidative phosphorylation (Say et al. 2012). Histologic and ultrastructural examination supports this theory, showing cells containing a cytoplasm that is filled with an overabundance of structurally abnormal mitochondria (Biggs and Font 1977; Eglen 1982; Morgan et al. 1998; Say et al. 2012). It has been suggested these altered mitochondria cause metabolic disturbances that play a key role in the formation of these tumors (Morgan et al. 1998; Say et al. 2012).

Clinical Presentation

An oncocytoma typically presents in elderly individuals as a red-tan, painless mass that has developed in the ocular adnexa over a period of several months (Biggs and Font 1977; Eglen 1982; Morgan et al. 1998; Say et al. 2012). The majority of ocular oncocytomas occur in the caruncle, and most are well-circumscribed, vascular nodules that appear to be subepithelial (Morgan et al. 1998; Say et al. 2012). Other clinical features may vary with the anatomic location of the tumor. Oncocytic lesions arising in the orbit have presented with unilateral proptosis, while those arising in the lacrimal sac have presented with unilateral epiphora, recurrent dacryocystitis, and a palpable mass in the lacrimal sac (Biggs and Font 1977; Say et al. 2012). All reported cases of ocular oncocytomas have been unilateral and solitary (Say et al. 2012).

Diagnosis

While oncocytomas have a typical clinical presentation, microscopic examination is required to make a definitive diagnosis. Histologically, these cells have a darkly eosinophilic cytoplasm arranged in a glandular pattern and frequently contain cystic spaces of inspissated amorphous material (Biggs and Font 1977; Eglen 1982; Morgan et al. 1998; Say et al. 2012). Electron microscopy shows an overabundance of abnormally shaped mitochondria in the cytoplasm (Biggs and Font 1977; Eglen 1982; Morgan et al. 1998; Say et al. 2012).

Differential Diagnosis

Nevus, conjunctival cyst, and melanoma

Prophylaxis

There is no known prophylaxis for oncocytomas.

Therapy

Treatment of oncocytomas is by local surgical excision with or without cryotherapy. With rare exception, benign oncocytomas do not recur after they are removed (Say et al. 2012).

Prognosis

Excellent. As stated above, local excision is typically curative for benign oncocytomas.

Epidemiology

Ocular adnexal oncocytic lesions are estimated to occur at a rate of 0.3 per million people per year (Say et al. 2012). Oncocytomas most often arise in

the seventh decade of life and are more common in women (Biggs and Font 1977; Morgan et al. 1998).

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One-and-a-Half Syndrome

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Synonyms

Fisher's one-and-a-half syndrome

Definition

The one-and-a-half syndrome is a clinical disorder of extraocular movements characterized by a conjugate horizontal gaze palsy in one direction plus an internuclear ophthalmoplegia (INO) in the other direction (Fisher 1967). The syndrome is usually due to a single unilateral lesion of the paramedian pontine reticular formation (PPRF) or the abducens nucleus on one side (causing the conjugate horizontal gaze palsy), with interruption of internuclear fibers of the ipsilateral medial longitudinal fasciculus (MLF) after it has crossed the midline from its site of origin in the contralateral abducens nucleus (causing failure of adduction of the ipsilateral eye) (Wall and Wray 1983). There is also a contralateral horizontal dissociated abducting eye nystagmus on attempted horizontal gaze.

Etiology

One-and-a-half syndrome can be caused by any lesion in the pons including multiple sclerosis (MS), brain stem stroke, brain stem tumors, and arteriovenous malformations (Wall and Wray 1983).

Occurrence

The one-and-a-half syndrome can affect patients of any age, either gender, or any race depending on structural etiology.

Cross-References

- ▶ Doll's Head Maneuver/Phenomenon, in Horizontal Gaze Palsy
- ▶ Internuclear Ophthalmoplegia
- ▶ Nystagmus
- ▶ Oscillopsia

Further Reading

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Onychoosteodysplasia (Nail-Patella Syndrome)

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Synonyms

Fong disease; Nail-patella syndrome; NPS; NPS1; Turner-Kieser syndrome

Definition

Onychoosteodysplasia is defined primarily by dysplasia of the nails, or absent or hypoplastic patellae. Other features include iliac horns, abnormality of the elbows interfering with pronation and supination, as well as nephropathy that resembles glomerulonephritis. The disorder is also associated with primary open-angle glaucoma.

Etiology

The disorder is caused by a heterozygous mutation in the LIM-homeodomain protein LMX1B on chromosome 9q34. Lmx1b has a crucial role in dorsal-ventral patterning of the vertebrate limb. Mouse models with LMX1B disruption demonstrate skeletal defects, hypoplastic nails, absent patellae, and renal dysplasia.

Clinical Presentation

The majority of patients presents with skeletal or nail abnormalities, which are present within the first several years of life. Primary open-angle glaucoma is found in 7–31% of NPS1 patients, with a mean age of presentation around 48 years. Lichter and colleagues identified cosegregation of POAG and NPS.

Diagnosis

Prenatal ultrasound has been used for third-trimester diagnosis of NPS, although its clinical utility is limited given the incidence of renal failure of less than 25% in patients. Ultrasound appears to have little prognostic value in diagnosis of NPS1. The disorder can be diagnosed through mutations in the LMX1B gene, although commercial assays are not available at the time of this publication.

Differential Diagnosis

Small patella syndrome (ischiopatellar dysplasia), patella aplasia-hypoplasia, Meier-Gorlin syndrome, genitopatellar syndrome, DOOR syndrome, Coffin-Siris syndrome, RAPADILINO syndrome, Rothmund-Thomson syndrome, Senior-Løken syndrome.

Prophylaxis

Eye screening exams are recommended from an early age, as soon as patients are able to tolerate slit-lamp examination, tonometry, and gonioscopy.

Therapy

Medical therapy with topical ocular antihypertensives and/or surgery may be recommended to manage POAG associated with NPS.

Prognosis

Primary open-angle glaucoma tends to manifest in the fourth decade of life in NPS, with a mean age

of presentation in the late 40s. There is not enough data to demonstrate the likelihood of progression of the glaucoma to requiring surgery or damage to the optic nerve with visual field loss. Optical coherence tomography and Humphrey visual fields can be used as part of routine screening to assess for potential vision loss as part of the annual examination with patients with NPS. Patients should also be monitored for the presence of proteinuria, which can indicate ongoing glomerulonephritic damage from renal dysplasia.

Epidemiology

Skeletal and nail abnormalities are present from childhood, while primary open-angle glaucoma does not manifest until patients are in their late 40s. There is no racial or geographic predisposition to NPS.

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Open Globe

► Corneoscleral Laceration

Open-Angle Glaucomas

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Definition

It is vitally important to recognize that the title is "glaucomas" not "glaucoma." This establishes the key concept that although glaucoma is defined by the characteristic changes in structure and function of the optic nerve, there are multiple, different underlying causes that result in the disease we call glaucoma (American Academy of Ophthalmology 2012). Many of the contributory factors have been identified, but we hope there are many more that will be identified going forward that will give us greater insight into the pathophysiology and treatment of this potentially blinding condition. In open-angle glaucomas, there is the additional requirement that trabecular meshwork be visible on gonioscopy. Open-angle glaucomas (OAG) are generally divided into primary and secondary causes. Primary (POAG) implies that no known underlying cause can be identified, whereas secondary implies that at least there is support for an identifiable underlying etiology for the optic nerve damage such as pigment dispersion, steroid-induced or exfoliation syndrome (Ritch et al. 1996).

Epidemiology

The World Health Organization estimated the incidence of POAG to be 2.4 million persons per year with the prevalence of blindness to be four million worldwide. Glaucoma was calculated to be the cause of 12.3% of blindness, making it the second leading cause worldwide. OAG has a prevalence of between 0.8% and 7.0% of the adult population, with a significant increase in older individuals and specific ethnic groups. The prevalence among individuals of African or Latino heritage is up to four times greater than

Caucasians; these patients have a greater risk of blindness as well.

Etiology

Open-angle glaucoma is often associated with elevated intraocular pressure (IOP). The increased levels of IOP are essentially always a result of decreased outflow rather than increased aqueous humor production. The decreased outflow is thought to be related to decreased flow through the trabecular meshwork, with the juxtacanalicular tissue being the site of greatest resistance. Once in the canal of Schlemm, there remains some resistance that is further increased in conditions that result in elevation of the episcleral venous pressure.

It is the susceptibility of the optic nerve to damage that ultimately determines if glaucoma is present. This damage affects the axons that comprise the optic nerve and may cause focal and diffuse loss. Focal loss is generally more easily identified and is more common in the superior and inferior poles of the optic disc. In those with normal tension glaucoma (NTG), damage occurs at what would otherwise be "normal" levels of IOP. In those with ocular hypertension, it is presumed that the optic nerve is better able to tolerate elevated IOP and no damage is observed (Alligham 2005).

Clinical Presentation

OAG has been referred to as the "sneak thief of sight" as there are usually minimal if any symptoms until late in the course of the disease. As a chronic disease, the loss of visual field tends to be slow and gradual, primarily affecting the peripheral vision. Many patients adapt to this loss and are unaware of it until it is of such severity that it affects their central vision. Multiple population-based studies have shown that at least 50% of the individuals with glaucoma have not been diagnosed. Since there are essentially no symptoms, an examination is required to make the diagnosis. Factors that increase the risk of developing glaucoma include older age, a positive family history of glaucoma, and African or Latino ancestry (Shaarawy et al. 2009).

Diagnostics

Gonioscopy with visualization of the anterior chamber angle is necessary to make the diagnosis of OAG and differentiate it from angle closure. It also allows identification of potential causes of secondary OAG including increased pigmentation in pigmentary glaucoma, a Sampaolesi's line in exfoliation syndrome, or neovascularization in early neovascular glaucoma. It is preferable to use a 4-mirror lens such as the Posner or Zeiss to facilitate compression gonioscopy. www.gonioscopy.org is an excellent site for further information.

Visual fields measure the functional performance of the visual pathway. In glaucoma, nerve fiber layer defects consistent with damage to the optic nerve are the typical focal findings. Unfortunately, static perimetry is not a very sensitive test to detect early damage. It has been shown that substantial loss of the optic nerve can occur prior to evidence of visual field loss. With severe damage, functional measurements may be more appropriate to determine progression.

Optic disc photographs and nerve fiber layer imaging are very useful to establish the baseline characteristics of structure and evaluate progression. Combined with a critical high magnification, stereoscopic examination, these allow early diagnosis, usually before visual field loss, and can identify increased risk of progression due to the presence of disc hemorrhages or beta-zone parapapillary atrophy.

Tonometry allows measurement of the IOP and can help determine the potential risk of developing glaucoma in the ocular hypertensive patient as well as determine the impact of therapy. Applanation tonometry results can be affected by central corneal thickness; however the exact magnitude of the impact is not currently known.

Comprehensive eye examination allows for the identification of possible etiologies of secondary glaucomas such as iris transillumination defects

and iris neovascularization. Pupillary examination for an afferent pupillary defect can help identify those with asymmetric optic nerve damage.

Differential Diagnosis

Historically, there has been great controversy as to whether normal tension glaucoma (NTG) represents just a part of the spectrum of open-angle glaucomas or is in fact a separate disease. It is defined as glaucomatous damage that occurs at an IOP $\leq$ 21 mm Hg. Since the level of IOP is not part of the definition of glaucomas, NTG is an OAG; however, in many instances the presence and frequency of specific findings and risk factors such as optic disc hemorrhages, systemic hypotension, and an early presentation of dense, paracentral scotomas tend to be different than POAG.

Prophylaxis

The Ocular Hypertension Treatment Study (OHTS) demonstrated a reduction of risk of developing POAG in patients with ocular hypertension with a 20% reduction in IOP. The decision to treat patients with elevated IOP and no glaucoma damage is individualized and based upon risk factors identified in OHTS and the European Glaucoma Prevention Study. A risk calculator is available: http://ohts.wustl.edu/risk/calculator.html

Therapy

Currently, the only modifiable risk factor is IOP. IOP reduction in OAG can be effectively accomplished with topical medications, laser trabeculoplasty, and surgical intervention. Medications can decrease aqueous humor production (beta-adrenergic blockers, carbonic anhydrase inhibitors, alpha-adrenergic agonists) or increase aqueous humor outflow (prostaglandin analogs, alpha-adrenergic agonists). Laser trabeculoplasty increases outflow through the trabecular meshwork. Filtration surgery increases aqueous outflow by either by passing at the normal outflow mechanisms (tube shunts, guarded filtration) or by improving flow through the canal of Schlemm. Multiple studies that include a wide range of patients with OAG have shown the consistent benefit of therapy in decreasing the risk of developing glaucoma or slowing the progression of existing glaucoma (Gross 2001).

Prognosis

The risk of developing POAG has been shown to be increased due to elevated IOP, increasing age, thin central corneal thickness, positive family history, and ethnicity. The risk of progressive glaucoma damage has been shown in multiple studies to be reduced with IOP reduction. In general, the lower the IOP, the less the risk of progression. Additional factors that increase the risk of progressive damage include optic disc hemorrhages, increasing age, more advanced visual field loss, and African ancestry.

Cross-References

- ▶ Angle Recession Glaucoma
- ▶ Primary Open-Angle Glaucoma
- ▶ Pigmentary Glaucoma

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Ophthalmic Astigmatism

- ▶ Astigmatism

Ophthalmic Division of the Trigeminal Nerve

▶ V1 (Ophthalmic Nerve)

Ophthalmic Migraine

▶ Retinal/Ocular Migraine

Ophthalmic Nerve

▶ V1 (Ophthalmic Nerve)

Ophthalmic Viscosurgical Device (OVD)

▶ Hyaluronic Acid, for Dry Eye
▶ Viscoelastic Agents

Ophthalmic Viscosurgical Devices

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Synonyms

Viscoelastic substances

Definition

Ophthalmic viscosurgical devices (OVDs) are a class of gel-like, clear substances with different quality characteristics that are used in refractive and intraocular surgery for safer maneuvers in the anterior and posterior chamber. OVDs differ in the rheologic polymer type(s), concentration, and chain length. They are commonly based on sodium hyaluronate, and their different qualities determine their physical and chemical condition, e.g., viscosity, elasticity, and cohesion.

Epidemiology

OVDs are not commonly used in ophthalmic surgery. Its use is subjected in difficult cases and depends on the decision of the surgeon.

History

In 1976 the first commercially available viscoelastic substance sodium hyaluronate (Healon) gained a US Investigational New Drug Application. The explicit perception ophthalmic viscosurgical device was created years later in 2000 by Arshinoff. OVDs were first introduced to maintain space in the eye during the implantation of intraocular lenses. With the development of different properties, additional functions of OVDs were introduced, e.g., protection of corneal endothelium or stabilization of the iris and pupil in patients with an iris floppy syndrome.

Clinical Features

Perfect OVDs should have the possibility to remain in the eye during the surgery and can be removed easily at the end of the process. In former times ophthalmic viscosurgical devices were either cohesive or dispersive depending on their molecular weight, concentration, and viscoelastic profile. Modern OVDs have due to their physical and chemical properties the ability to change from a viscous cohesive profile at low shear rate to fracturable at higher shear rates. This accomplishment is called viscoadaptivity. However, despite having wide spectra in its use, OVDs are not

without well-known side effects as there are intraocular pressure elevation and wound burns.

Etiology

See "History" section above.

Treatment

With the development of different kinds of OVDs with different viscoelastic properties, many branches of appropriateness have been developed. OVDs are used to maintain the space in the eye, they have the ability to protect the corneal endothelium, and they have an inhibitory effect against free radical formation and platelet aggregation. They are used for complicated cataract surgery cases, and their indications have expanded to other surgeries such as corneal lamellar surgery and glaucoma surgery. They are of an important use in intraoperative floppy iris syndrome and capsulorhexis in intumescent and pediatric cataracts.

Cross-References

- ▶ Anterior Chamber
- ▶ Intraoperative Floppy-Iris Syndrome
- ▶ Posterior Chamber

Further Reading

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Ophthalmodynia Periodica

- ▶ Ice Pick Pains

Ophthalmoplegia, Internuclear

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Definition

Internuclear ophthalmoplegia (INO) is a disorder of conjugate horizontal gaze. When a patient with INO is asked to move their eyes horizontally, the eye contralateral to the gaze direction will be unable to adduct, and the eye ipsilateral to the gaze direction will demonstrate nystagmus. For example, a right INO will present with left eye nystagmus and an inability of the right eye to adduct upon gaze to the left (Hickey 2003).

Etiology

INO is caused by damage to the medial longitudinal fasciculus (MLF), a fiber tract that extends from the rostral midbrain to the spinal cord. The MLF contains many important tracts including the pathway connecting the abducens nucleus and oculomotor nucleus, which is important for coordinating the eyes during horizontal

conjugate gaze (Riordan-Eva and Hoyt 2011). For example, a patient with right INO will have damage to the right MLF, preventing communication between the left abducens nucleus and the right oculomotor nucleus. As the patient tries to look to left, the left eye will abduct, but the right eye will remain stationary (Hortan 2012). In addition, the left eye will demonstrate horizontal nystagmus due to cortical eye movement control centers attempting to compensate for the lack of adduction of the right eye (Riordan-Eva and Hoyt 2011).

Occurrence

INO can be caused by many conditions including multiple sclerosis (MS), brainstem infarction, tumors, arteriovenous malformations, Wernicke's encephalopathy, and encephalitis. INO ranges from a mild form where the adducting eye moves slower than normal resulting in transient diplopia to a severe form where there is constant diplopia upon lateral gaze. In a young patient with a bilateral INO, one would suspect MS, whereas in an older patient, one would instead suspect brainstem infarction (Riordan-Eva and Hoyt 2011).

Classification

None

Cross-References

- ▶ Diplopia in Vertebrobasilar System Disease
- ▶ Efferent Visual system (Ocular Motor Pathways)
- ▶ One-and-a-Half Syndrome
- ▶ WEBINO ("Wall-Eyed" Bilateral Internuclear Ophthalmoplegia) Syndrome

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Optic Atrophy

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Synonyms

Optic neuropathy

Definition

True optic atrophy is a pathologic description of the ophthalmoscopic finding of axon loss at the optic nerve head. The nerve fiber layer and visible optic nerve change can be caused by any lesion along the anterior visual system pathway (retinogeniculate) from the retina to the lateral geniculate nucleus (LGN). Optic atrophy is not a disease by itself, but rather a sign of various disorders in the anterior visual system. Sometimes, an optic nerve appears atrophic but does not have true nerve fiber layer loss (e.g., physiologic optic disc pallor).

Symptoms of Optic Atrophy

Cranial nerve (CN) II is composed of a bundle of nerve fibers that originate in the retina, exit the eye at the optic disc, and then project to the optic chiasm, optic tract, and then the lateral geniculate body. Optic atrophy is typically a sign of ipsilateral retinopathy or optic neuropathy but can result from any lesion anterior to the cell body (e.g., optic chiasm and optic tracts) in the lateral geniculate body.

Thus, patients with optic atrophy can present with visual acuity loss, visual field defect, dyschromatopsia, decreased contrast sensitivity, dimness or decreased light brightness, or complete blindness.

Clinically, optic atrophy presents as an ophthalmoscopically visible change in the color and structure of the optic disc. A healthy optic disc is typically a yellow-pink to reddish color but changes to a washed-out, pale color when it atrophies. These changes are associated with varying degrees of vision loss or dysfunction and may be found as an incidental finding in some cases.

Patients with nasal nerve fiber loss (corresponding to temporal visual field loss) can develop a band of atrophy across the optic nerve called "band" or bowtie optic atrophy. Thus, patients with a bitemporal hemianopsia might have bilateral band atrophy, and patients with a homnonymous hemianopsia from an optic tract lesion can have band atrophy in the eye with the temporal visual field loss (corresponding to the nasal fiber loss in the optic nerve).

Etiology

Many diseases can lead to damage or atrophy of the optic nerve, so it is important to discover the specific cause, for example, glaucoma (usually producing cupping of the disc rather than optic atrophy per se):

- Retinopathy and retinal vascular disease
- Multiple sclerosis (demyelinating optic neuropathy)
- Ischemia (e.g., ischemic optic neuropathy)
- Trauma (traumatic optic neuropathy)
- Inflammatory (e.g., sarcoidosis and vasculitis)
- Infiltrative (leukemic and other malignancies)
- Compression (e.g., pituitary, brain, or optic nerve tumors)
- Toxic (e.g., ethambutol, heavy metals, methanol) exposure or nutritional deficiencies (e.g., B12 or folate deficiency)
- Infections (e.g., syphilis, tuberculosis, Lyme disease, meningitis)
- Congenital, hereditary, or other genetic causes

The mode of onset of visual deficits can be an important indicator of the cause of the optic atrophy. Rapid or acute onset is more typical of ischemia, demyelination, inflammation, and trauma. A gradual onset over several months can be due to compressive tumor, toxic exposure, or nutritional deficiencies.

Occurrence

Some studies show that the prevalence of all blindness attributable to optic atrophy is between 0.04% and 0.8%. Thus of all the probable causes, less than $<1\%$ of all blindness is caused by optic atrophy.

Treatment

Unfortunately, optic atrophy per se cannot be reversed, but there may be variable recovery of function following treatment of the underlying etiology.

Prognosis

The prognosis depends upon the underlying etiology.

Cross-References

▶ Optic Nerve (Cranial Nerve II)

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Optic Disc

▶ Fundamental Considerations Regarding the Optic Nerve

Optic Disc (Optic Nerve Head)

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Synonyms

Optic nerve head

Definition

The optic disc is the most anterior (or distal) portion of the optic nerve and extends from the surface of the retina to the myelinated portion of the optic nerve, which begins just behind the sclera. It is composed of about 1.2 million nerve fibers (axons) that originate in the ganglion cell layer of the retina.

Basic Characteristics

The optic disc is located nasal to and slightly superior to the macula and is an aggregation of fibers of the retinal nerve fiber layer as they exit the intraocular space through the sclera to form the optic nerve. Retinal ganglion axons bend acutely as they enter the optic nerve and are divided into about 1000 fascicles. They then pass through one of a few hundred holes that perforate the lamina cribrosa, the collagenous fenestrated support of the optic disc. The blood supply of the optic disc is the central retinal artery anteriorly but shifts to branches of the ophthalmic artery posteriorly. The average size of the optic disc is 1 mm in the anterior-posterior dimension, 1.5 mm horizontally, and 1.8 mm vertically; however, there exists a wide variation of dimensions seen in normal individuals.

The optic disc has a central depression, or a physiologic cup, which is typically one-fourth to one-third the width of the optic disc and located approximately centrally. The cup is small or nonexistent in small optic discs and can be larger (and still considered normal) in eyes with larger optic discs. The cup-to-disc ratio is a typical way of recording the appearance of the optic disc and is the ratio of cup diameter to disc diameter. The ISNT rule describes the normal appearance of the optic nerve regarding the relationship between the rim thickness of the inferior, superior, nasal, and temporal aspects of the optic disc. The ISNT rule says that the inferior rim should be as thick or more thick than the superior rim which should be as thick or more thick than the nasal rim which should be as thick or more thick than the temporal rim. So in a normal disc, the thickest rim should be the inferior rim, and the others are gradually thinner with the temporal being the thinnest (I → S → N → T). Violation of the ISNT rule should raise suspicion about the presence of glaucoma, in part because in glaucoma the superior and inferior poles are particularly susceptible to damage which can result in relative thinning of one of these rims. For example, if the inferior rim is thinner than the superior rim, there should be suspicion for the presence of glaucoma. The utility of applying the ISNT rule to help detect glaucoma has been supported by research. Aside from the cup-to-disc ratio and the location of the cup relative to the rims of the optic disc, the appearance of the optic disc rim, or the area of the optic disc surrounding the cup, is important. For example, pallor of the optic disc rim, the presence of hemorrhages, abnormal blood vessels, or swelling may help differentiate between diagnoses. It is

recommended that a detailed description of the optic disc be recorded in the medical record, either via drawing or photography.

The optic disc is susceptible to elevated intraocular pressure which can cause glaucomatous optic atrophy characterized by enlargement of the optic disc cup over time or progressive cupping. Progressive cupping may be concentric or appear as a more localized change with focal notching of the rim of the optic disc (hence the ISNT rule). Other forms of optic atrophy cause pallor without increased disc cupping. The development of inferior or superior thinning of the optic disc rim in glaucoma may have a physiologic basis. The mechanical theory holds that because the lamina cribrosa is poorly supported at the superior and inferior edges of the disc, pressure forces acting on the lamina cribrosa may cause the initial damage. Alternatively, microcirculatory abnormalities may play a role in the development of glaucoma.

Optic disc edema occurs when axoplasmic transport of materials needed to maintain the axons of the optic nerve is blocked. Disc edema can be associated with increased intracranial pressure, ocular hypotony, increased intraocular pressure, tumors, or central retinal vein occlusion. Some clinical signs of optic disc edema are blurring of the optic disc margins, decrease in size or loss of the cup, venous congestion, papillary and peripapillary hemorrhages, and hyperemia of the optic disc.

Cross-References

► Optic Nerve (Cranial Nerve II)

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Optic Disc in Central Retinal Vein Occlusion

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Definition

Optic disc edema can occur in central retinal vein occlusion (CRVO) or hemicentral retinal vein occlusion (HCRVO). Depending on the type and severity of the occlusion, the optic disc may be at risk of developing edema, disc neovascularization (NV), retinochoroidal venous collaterals (optociliary shunt vessel), and disc hemorrhages. Conversely, the anatomy of the optic disc and its surrounding vascular structures can play a role in the development of CRVO and HCRVO.

Etiology

The optic disc is the site of arterial inflow and venous outflow for the retina, with the central retinal artery and vein exiting the eye down the middle of the optic nerve. In most patients, occlusion of this vein results in CRVO. However, in 20% of the population, there are two trunks of the central retinal vein that exit the eye at the optic disc.

Occlusion of only one of these trunks results in HCRVO, leaving half of the retina unaffected. There are two distinct categories of both CRVO and HCRVO, ischemic and nonischemic (sometimes referred to as venous stasis retinopathy). The etiology of any retinal vein occlusion (CRVO, HCRVO, BRVO) is typically multifactorial in origin. However, in younger patients evidence suggests that optic disc vasculitis or hypercoagulable state may be responsible for the thrombosis in RVO.

Edema of the optic disc is a relatively common sign of CRVO/HCRVO. NV of the optic disc (NVD) may occur in ischemic RVO cases and is believed to be the result of vascular growth-promoting cytokines (e.g., FGF, VEGF, Ang1, Ang2, PDFG) released by tissue in response to an ischemic environment. These immature and leaky blood vessels (NV) can subsequently hemorrhage into the vitreous.

Venous disc collaterals can occur in ischemic or more commonly in nonischemic CRVO/HCRVO and may be seen as the only sign in otherwise asymptomatic nonischemic RVO patients. Thus, it has been proposed that collateral formation is evidence of the gradual nature by which some retinal vein occlusions form. It is believed that disc collaterals form between the retinal and choroidal circulation by expansion or recanalization of existing vascular channels in order to bypass the venous occlusion further downstream.

Clinical Presentation

Patients with CRVO may present with sudden unilateral blurred vision. Symptoms are often noticed upon waking up in the morning. In "impending" nonischemic CRVO, the blurring is relatively mild in the morning, but gets better throughout the day. In ischemic CRVO, the vision loss is sudden and severe. In HCRVO, these symptoms are similar, but vision loss may only affect half of the patient's visual field.

Vascular abnormalities of the optic disc such as neovascularization and collaterals can usually be identified with ophthalmoscopy, but can be more easily distinguished with fluorescein angiography (FA). Some nonischemic CRVO/HCRVO patients with disc collaterals may be relatively asymptomatic.

Diagnostics

Indirect or direct ophthalmoscopy can identify swelling of the optic disc, neovascularization, and disc collaterals. OCT should be used to confirm and quantify the presence of disc edema. In patients with suspected CRVO/HCRVO, FA imaging can be used to evaluate the overall status of the retinal vasculature. In relation to disc pathology, FA can evaluate neovascularization, flow through venous collaterals, and non-perfusion of the surrounding retina. Fundus autofluorescence imaging can detect in patients with recent ischemic CRVO a perivenular hypoautofluorescence.

Differential Diagnosis

Retinal vasospasm, migraine, uveitis, closed-angle glaucoma, optic neuritis, and papilledema

Prophylaxis: Treat Risk Factors

Therapy

Treatment should be directed at underlying etiology (e.g., hypertension). Treatment of complications including NV glaucoma and elevated intraocular pressure should be considered.

Anti-VEGF agents have also been proven to be helpful in RVO.

Prognosis

In nonischemic CRVO/HCRVO, the prognosis is relatively good with about 50% of patients having their vision return to normal. However, the chance of converting from nonischemic to ischemic is about 13% in within 18 months. This risk increases with age. In ischemic CRVO/HCRVO, the prognosis is much worse due to permanent damage from macular ischemia. There is also a high risk of neovascular glaucoma (NVG).

Cross-References

► Diabetic Disc Edema

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Optic Disk

► Optic Nerve (Cranial Nerve II)

Optic Gliomas

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Definition

An optic nerve glioma (ONG) is a rare tumor of the glial cells of the optic nerve. It is usually a pilocytic tumor that may also affect the optic chiasm or optic tract and rarely regresses spontaneously. ONG may cause swelling or atrophy of the optic nerve.

Etiology

Most ONGs are slow growing and histologically benign and occur most commonly in children. ONGs are associated with neurofibromatosis type 1 in up to 30% of patients.

Clinical Presentation

Symptoms include painless, progressive vision loss, proptosis, strabismus, and optic nerve edema or atrophy.

Therapy

Treatment may not be necessary and observation is the recommended first step in ONG especially in cases of NF1. Chemotherapy and in older children radiation therapy are options for patients with clinical and/or radiographic progression. Surgical resection usually results in worsening or complete visual loss and is not generally recommended in seeing eyes. Patients however with nonuseful vision, severe pain, or severe proptosis might benefit from surgical resection or debulking.

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Optic Nerve (Cranial Nerve II)

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Synonyms

Cranial nerve II (CN II); Optic disk; Optic nerve head

Definition

The optic nerve ON (cranial nerve II) is an afferent sensory nerve that transmits visual input from the eye to the occipital cortex. The second of 12 paired cranial nerves, the optic nerve is unique because it is part of the central nervous system and develops from the diencephalon. The ON is surrounded by the meninges of the optic nerve sheath and is myelinated by oligodendrocytes. The ON consists of an average of 1.2 million axons originating from the retinal ganglion cells in the retinal nerve fiber layer which receives visual input from photoreceptors in the retina. The ON is approximately 1.5 mm in diameter and enlarges to 3.5 mm posterior to the lamina cribrosa because of the myelin nerve sheath, which protects and insulates the nerve. The optic nerve about is 45–50 mm long and consists of four portions: intraocular, intraorbital, intracanalicular, and intracranial. The intraocular portion (1 mm), also known as the optic nerve head (or optic disk), lies within the eye and is unmyelinated; this segment of the optic nerve is supplied by the short posterior ciliary arteries from the ophthalmic artery. The intraorbital segment (25 mm) extends from the posterior globe to the optic canal and is thicker in diameter because the optic nerve becomes myelinated posterior to the lamina cribrosa and is supplied by the ophthalmic artery. The intracanalicular segment (9 mm) traverses the optic canal along with the sympathetic plexus and the ophthalmic artery; it is supplied by the ophthalmic artery. The intracranial segment (15 mm) extends from the optic canal to the optic chiasm, and it is supplied by the internal carotid artery, anterior cerebral, and anterior communicating arteries.

The optic nerves from both eyes converge at the optic chiasm of the visual pathway and then separate into the optic tracts, which lead to the lateral geniculate nucleus (LGN) and the visual cortex in the brain. Damage to the optic nerve may cause permanent loss of vision, including visual acuity or visual field loss. Injury located anterior to the optic chiasm causes ipsilateral visual field defect.

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Optic Nerve Decussation

▶ Wilbrand Knee

Optic Nerve Edema

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Optic Disc Edema

Swelling of the optic disc occurs when there is obstruction of axonal transport at the level of lamina cribrosa, which may result from compression, ischemia, inflammation, metabolic, or toxic reactions.

Papilledema means optic disc elevation due to increased intracranial pressure. Usually it is bilateral and symmetric, but it may be asymmetric or even unilateral.

The appearance of the optic disc in papilledema is indistinguishable from disc edema resulting from other causes. Regardless of its cause, the following clinical features of optic disc edema may be observed: elevation of the nerve head with variable filling in the physiologic cup; retinal vessels may appear to drape over the elevated disc margin, blurring of the disc margins, peripapillary nerve fiber layer opacifications, the retinal nerve fiber layers become grayish white, and opalescent margins obscuring portions of retinal vessels; hyperemia and dilatation of disc surface, retinal venous dilatation, and tortuosity; peripapillary hemorrhages, exudates or cotton wool spots, and retinal folds or macular edema.

The ophthalmoscope appearance of papilledema helps classify it into four stages:

1. Early papilledema – there is minimal hyperemia, swollen of the superior and inferior pole, and absence of spontaneous venous pulsations.
2. Full-blown papilledema – there is swollen of optic disc with hemorrhages and exudates, and the edematous peripapillary retinal nerve fiber layer is grayish white and opalescent that obscures the disc edge and retinal vessels within.
3. Chronic papilledema – hemorrhages and exudates are scarce, but capillary telangiectasia is evident on disc surface.
4. Atrophic papilledema – optic disc pallor.

Patients with papilledema may complain of transient obscurations of vision, which may occur in one or both eyes, typically lasting seconds; visual acuity loss is a late finding.

Visual field reveals only enlargement of the blind spots in the early stages of papilledema; in the more chronic forms, visual field defects appear most frequently as those of the inferior nasal nerve fiber bundle defects.

Optic Nerve Head

▶ Fundamental Considerations Regarding the Optic Nerve
▶ Optic Disc (Optic Nerve Head)
▶ Optic Nerve (Cranial Nerve II)

Optic Nerve Head Drusen

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Optic Nerve Head Drusen

Optic nerve head drusen represent refractile, often calcified nodules located within optic nerve head.

The prevalence ranges from 0.34% in clinical settings to 2% in autopsy studies. Optic nerve head drusen are often bilateral (75–86%), but can be asymmetric.

The pathophysiology of optic nerve head drusen is unclear, most theories suggesting impaired ganglion cell axonal transport, probably related to a small scleral canal and mechanical obstruction, metabolic abnormalities associated with impaired transport, which may result in intra-axonal mitochondrial damage over time with subsequent calcification of the extruded.

Most patients with optic nerve head drusen do not experience symptoms; however, few patients (8.6%) may have transient visual obscuration. Visual fields defects remain either stable or worsen slowly.

The optic discs of patients with optic nerve head drusen appears elevated with indistinct or irregular margins and with an anomalous vascular branching pattern.

In childhood, optic nerve head drusen begin buried, and over the years the drusen become more discernible. When become visible, optic nerve head drusen appear as round whitish-yellow refractile bodies.

Ancillary tests: ultrasonography – calcified drusen maintain high echogenicity and do not produce widening of the intraorbital nerve.

Neuroimaging – on computerized tomography, calcified drusen can be seen as a bright signal at the junction of posterior globe and optic nerve.

Optical coherence tomography – it can show the discrete hyperrefractive drusen, but these are not evident in all cases.

Optic Neuritis

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Definition

Multiple sclerosis (MS) can lead to optic neuritis where demyelination and inflammation of the optic nerve causes vision change or vision loss.

Etiology

Optic neuritis (ON) in MS is caused by inflammatory demyelination of the optic nerve. Acutely, T-cell-mediated inflammatory release of cytokines leads to destruction of oligodendrocytes, while, chronically, B cells and microglia-related inflammation cause damage. Recovery can occur within days to weeks due to remyelination and redistribution of sodium channels; however, the recovery is not 100%, and the redistribution of the sodium channels can leave neurons more vulnerable to future insult.

Clinical Presentation

Up to 90% of patients with ON present with central vision loss in combination with dull retrobulbar, periocular, or mild orbital pain upon eye movement. A loss of color vision and contrast sensitivity often accompany the decline in visual acuity. Less commonly, patients present with peripheral vision loss, flashes, photophobia, and decreased depth perception. The swinging pen light exam will often demonstrate and a relative afferent pupillary defect unless both optic nerves are involved. Typically the fundoscopic exam initially is normal (i.e., retrobulbar optic neuropathy) but sometimes reveals a mildly swollen optic disk if the optic nerve lesion is anteriorly located.

Diagnostics

The primary means of diagnosing ON radiographically is magnetic resonance imaging (MRI) of the orbit and brain with fat suppression. This might show an enhancing ipsilateral optic nerve, and the brain MRI might show periventricular white matter lesions with or without enhancement.

Differential Diagnosis

Many other inflammatory or infiltrative diseases such as acute ischemic optic neuropathy, Leber hereditary optic neuropathy, granulomatous

inflammation, other autoimmune diseases, infection, severe sinusitis, neuroretinitis, posterior uveitis, vasculitis, malignancies, and paraneoplastic syndromes and cause optic neuritis-like symptoms.

Prophylaxis

Immunomodulatory therapy might reduce the number of MS attacks including recurrent ON.

Therapy

Much like MS, the mainstay therapy for optic neuritis due to MS is initial intravenous (IV) corticosteroids such as methylprednisolone followed by a course of oral corticosteroids. IV immunoglobulin has also been shown to have possible benefit and, in some rare cases of optic neuritis unresponsive to corticosteroids plasmapheresis, has been used. In the ONTT, IV steroids sped the rate of recovery but did not change visual outcome compared with oral steroids or placebo. Oral steroids in conventional doses however were associated with a higher rate of recurrence of ON and are not recommended in conventional doses for ON.

Prognosis

The symptoms of optic neuritis typically peak within a few days but take several weeks to fully disappear. More importantly, though, optic neuritis is an indicator of current MS or possible future onset of MS. According to the longitudinal Optic Neuritis Study Group, the 15 year probability for developing MS after optic neuritis is 50%, but in patients with multiple white matter lesions, the risk is higher (>70%) This probability increases with every white matter abnormality detected by MRI at the time of the optic neuritis episode.

Epidemiology

The incidence of unilateral optic neuritis is between 0.94 and 2.18 per 100,000 per year around the world with the incidence of bilateral optic neuritis much lower than unilateral optic neuritis.

Cross-References

- ▶ Demyelination, in Multiple Sclerosis, Optic Neuritis
- ▶ Poser Criteria, for Multiple Sclerosis
- ▶ Relative Afferent Pupillary Defect (RAPD)

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Optic Neuritis: Overview

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Synonyms

Demyelinating optic neuropathy; Idiopathic optic neuritis; Inflammatory optic neuropathy; Retrobulbar optic neuritis

Definition

The term optic neuritis (ON) for the purposes of this entry will refer to idiopathic or demyelinating dysfunction of the optic nerve.

Etiology

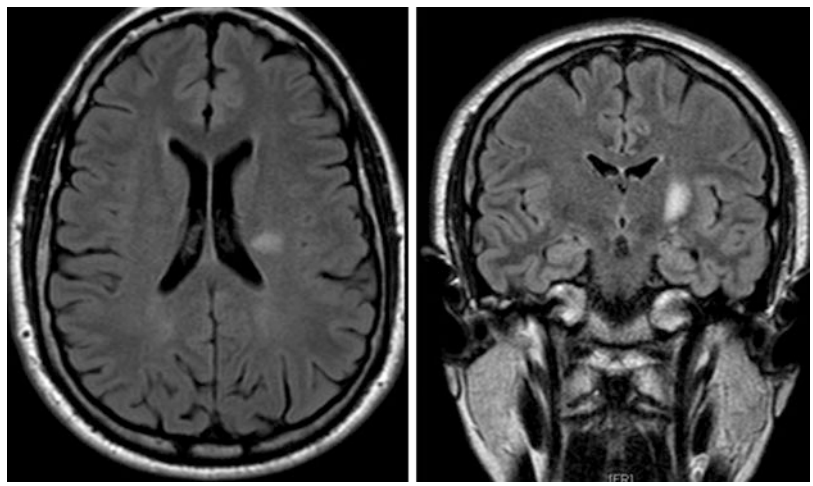
Although we use the term ON to typically describe idiopathic or demyelinating optic neuropathy, other optic neuropathies can result from non-demyelinating processes and can mimic the clinical presentation of ON. These optic neuropathies include autoimmune or inflammatory (e.g., systemic lupus erythematosus and sarcoidosis), infectious (e.g., cat scratch neuroretinitis), toxic (e.g., ethambutol), neoplastic or compressive (e.g., meningioma), nutritional (e.g., B12 or folate deficiency), ischemic (e.g., anterior ischemic optic neuropathy (AION)), and hereditary (e.g., Leber hereditary optic neuropathy (LHON)) disease. For the purposes of this entry, we reserve the term ON for idiopathic or demyelinating ON and prefer the term "optic neuropathy" for other non-ON etiologies (Fig. 1).

Clinical Presentation

The typical presentation of ON is acute to subacute (hours to days) onset of a unilateral, painful loss of vision (usually described as pain with eye movement in 92% of the cases). Demyelinating ON typically affects Caucasian adults between 15 and 45 years, but the epidemiology of ON is different depending on the incidence and prevalence of demyelinating disease (i.e., MS) compared with other etiologies (e.g., infectious). A female predominance is noted in ON in up to 75% of the cases, but ON may affect either gender. Although the majority of ON is unilateral at presentation in adults, bilateral cases are more common pediatric patients, and in some populations of non-European descent, the presentation of ON is often different (e.g., African, Indian, and Asian populations). In the Asian population, for example, ON may occur in the setting of an opticospinal presentation (neuromyelitis optica (NMO)) than typical "Western" MS.

In a large, National Eye Institute (NEI)-sponsored trial, the Optic Neuritis Treatment Trial (ONTT), the most common symptom of ON was central vision loss (92.2%), and the second most common symptom was pain, typically retro-orbital pain worse with eye movement (92%).

The visual acuity in ON is variable and may range from normal (20/20) to no light perception. A relative afferent pupillary defect (RAPD) is usually seen in the affected eye unless the disease is bilateral and symmetric. Color vision loss (dyschromatopsia) is also a common finding and may be out of proportion to the visual acuity loss. The visual field in ON is likewise variable and can



Optic Neuritis: Overview, Fig. 1 Fluid attenuation inversion recovery (*FLAIR*) T2-weighted magnetic resonance imaging of the head shows a typical periventricular white matter lesion consistent with demyelination

include ipsilateral central or any nerve fiber layer-type defect. Asymptomatic contralateral eye involvement may also be seen in patients presenting acutely with unilateral ON. The remainder of the ocular examination in ON is typically normal in demyelinating disease, and the presence of anterior or posterior segment inflammatory signs (e.g., uveitis) should prompt consideration for inflammatory or infectious etiologies. In addition, although clinically there is an optic neuropathy, the fundus is typically normal in demyelinating ON (e.g., retrobulbar optic neuropathy). Optic disc edema however can be seen in up to one third of cases, but typically the disc edema when present is only mild. The presence of severe disc edema, marked peripapillary hemorrhages, cotton wool patches, or retinal exudates with macular star should prompt consideration for non-demyelinating etiologies for the optic neuropathy.

Diagnostics

The diagnosis of ON is a clinical one, but further evaluation is recommended for patients with ON. In the United States, the primary recommended imaging modality for ON is magnetic resonance imaging (MRI) of the brain with gadolinium to evaluate for demyelinating disease. A concomitant orbital MRI with fat suppression and gadolinium might be useful to show enhancement of the optic nerve and to exclude alternative etiologies in atypical cases. Up to 94% of patients with active acute ON will show an enhancing (i.e., active) optic nerve on the post-contrast MRI, and the absence of this radiographic finding should make the diagnosis of typical ON suspect. Although rarely compressive etiologies may mimic the clinical presentation of ON (e.g., pituitary apoplexy or ophthalmic artery aneurysm), the primary purpose of the MRI in typical ON is for diagnostic and prognostic purposes for demyelination (i.e., MS).

The cranial MRI in MS may show the typical demyelinating periventricular, white matter lesions. These lesions are often transversely oriented, oval shaped, and located in key areas such as the corpus callosum. The presence of different aged lesions (enhancing T1-weighted MRI lesions versus other T2 lesions) may be useful for demonstrating radiographic dissemination in space and time. Cerebrospinal fluid (CSF) testing for oligoclonal bands and elevated immunoglobulin although not required in typical ON may be useful for supporting a diagnosis of demyelinating disease, but in general these decisions and discussions are best left to the consultant neurologist and not the ophthalmologist. In the ONTT, other laboratory testings (e.g., syphilis serology, antinuclear antibody, chest radiography) in typical ON cases did not provide any additional diagnostic information, and likewise in those patients who had undergone CSF analysis, no additional diagnosis beyond demyelinating disease was confirmed.

In contrast, atypical ON cases (e.g., painless, recurrent, bilateral, or non-recovering ON, marked disc edema, uveitis, macular star figure), laboratory and CSF analysis might be necessary. Patients with atypical ON should be evaluated for MS variants (e.g., neuromyelitis optica or Devic's disease) or MS mimics (e.g., sarcoidosis, syphilis, tuberculosis (TB), Lyme disease, systemic lupus erythematosus (SLE), etc.). Laboratory testing in these cases depending on the clinical presentation including complete blood count, antinuclear antibody, syphilis, Lyme or Bartonella serology, chest radiography, *angiotensin*-converting *enzyme* (ACE) and aquaporin-4-specific serum autoantibody (NMO), etc., could be considered.

Differential Diagnosis

1. Inflammatory optic neuropathy (e.g., sarcoidosis, lupus)
2. Infectious optic neuropathy (post-viral, syphilis, Lyme disease, TB)
3. Other optic neuropathies (e.g., toxic, nutritional, compressive, ischemic, radiation induced, hereditary)

Prophylaxis

Not applicable.

Therapy

ON is a self-limiting disease and the visual loss typically resolves partly or completely. Although some cases have a residual visual deficit, this should be considered an atypical feature as most patients recover vision better than 20/40. In the ONTT, the intravenous (IV) corticosteroids 1 g per day for 3 days followed by an oral (PO) prednisone or taper to a total of 11 days sped the rate of recovery but did not change final visual outcome (which was good in all patients in the ONTT) compared with placebo or oral steroids alone. Interestingly however, oral steroids alone did increase the frequency of recurrent attacks of ON, and oral steroids in conventional doses are therefore not recommended for typical ON.

Prognosis

In the ONTT, at 15 years following onset of ON, patients with a normal brain MRI had a 25% risk of developing MS when compared to patients with demyelinating white matter lesions of MS who had a 72% risk of developing clinically definite MS at year 15. Thus, patients with ON who have a normal MRI at onset should not be told that they do not have MS (the ONTT risk of MS is 25% at year 15) and patients with an abnormal MRI should not be told that they do have MS (the ONTT risk of MS is 72% at year 15).

Epidemiology

Typically ON in the United States affects younger adults (age range from 20 to 40 years) with a strong female predominance (two-thirds) of the cases and a predilection for Caucasians. The annual incidence of ON in the United States is approximately 6.4 per 100,000, and the prevalence is 115/100,000. The incidence of ON is higher in the populations in the northern United States and Western Europe with higher latitudes and is lowest in regions closer to the equator. The demographics of ON is different globally however, and in some parts of the world (e.g., Asia), ON may be more likely to be idiopathic or infectious than demyelinating in origin and when demyelinating may be more likely to be of the opticospinal variant (NMO) compared with countries with populations of European descent.

Cross-References

- ▶ Sarcoidosis
- ▶ Syphilis: Overview

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Optic Neuropathy

- ▶ Optic Atrophy

Optic Neuropathy: Ischemic, Arteritic

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Definition

Ischemic optic neuropathy is the most common acute optic neuropathy in adults over the age of 50 years, accounting for many cases of blindness or seriously impaired vision in that age group; however, no age is immune as this disorder has been reported in younger patients as well, including children.

Etiology

A typical classification divides anterior ischemic optic neuropathy into an arteritic (AAION) and non-arteritic (NAION) variants, which has important clinical and prognostic implications. AAION is associated with temporal (giant cell) arteritis and NAION is often related to atherosclerosis.

Clinical Presentation

The typical presentation of both AAION and NAION is painless loss of vision typically associated with optic disk swelling accompanied by flame-shaped (splinter) hemorrhages. However, vision is usually much worse in AAION compared to NAION (light perception vs. 20/200 vision). The visual loss is commonly described as sudden but progression over several days is also possible. Some patients report on transient visual loss in the days to weeks preceding the event. NAION is presumed to result from circulatory insufficiency within the optic nerve head. Histological studies show the area of infarction is located within the sclera canal alone supporting thus the compartment syndrome theory.

Diagnosis

The diagnosis of anterior ischemic optic neuropathy is clinical and is based on typical findings including abrupt loss of vision, usually unilaterally, accompanied by swollen optic disk with splinter hemorrhages.

AAION is less frequent than NAAION accounting for approximately 5–10% of all cases of anterior ischemic optic neuropathy. AAION usually occurs in older patients, over the age of 70 years, and is related to inflammatory and thrombotic occlusion of the short posterior ciliary arteries. Many patients have systemic symptoms of temporal arteritis including headache, malaise, pain after chewing, and scalp tenderness. Typical findings in blood tests include elevated sedimentation rate and/or C-reactive protein levels, thrombocytosis, and anemia. Confirmation of the clinical suspicion of temporal arteritis requires a temporal artery biopsy that may be delayed for 7–10 days following initiation of steroid therapy.

In NAAION, visual loss is usually less severe than in AAION; it occurs over hours to days often described as blurring, dimness in the affected region of visual field, and with altitudinal defect as the most common visual field loss. The optic disk edema may be diffused or segmental hyperemic or pale. In NAAION, the optic disk in the contralateral eye is typically small in diameter and there is absent of physiologic cup (disk at risk).

Neuroimaging is usually unnecessary in typical cases; however, if atypical features exist, such as severe optic disk edema, bilateral presentation, young age, or associated pain, imaging is warranted.

Differential Diagnosis

1. Other optic neuropathies: optic neuritis, compressive optic neuropathy, inflammatory, and infectious optic neuropathies
2. Increased intracranial pressure (especially if there is bilateral involvement of both optic nerves)

Prophylaxis

There is no effective medical or surgical treatment for NAION or for prevention of second eye involvement following unilateral presentation. Control of vasculopathic risk factors (i.e., hypertension, hyperlipidemia, diabetes and smoking) and aspirin are usually advised; however, there is no evidence to support that they reduce the risk of occurrence of NAION in the initially uninvolved eye.

Following unilateral AAION, there is high risk for second eye involvement within days of presentation. Therefore, following unilateral AAION treatment with systemic steroids should be initiated promptly.

Therapy

NAAION: No effective therapy exists. Aspirin, control of underlying medical conditions, and avoidance of smoking are commonly recommended.

AAION: A common treatment regime is with intravenous methylprednisolone 1 g/day for 3 days followed by oral prednisone 1 mg/kg/day that is continued for 3–12 month and tapered slowly depending on the response and sedimentation rate.

Prognosis

Although the damage to the optic nerve is often permanent, mild improvement of vision is possible in the initial first months following the event. The typical visual field defect of NAION is an altitudinal defect, and in AAION, visual field constriction is usually worse, leaving a small island of vision if any. Up to 40% of patients with NAAION show spontaneous improvement in vision compared to presentation, but this is usually limited to several lines of visual acuity and residual damage is commonly present.

Epidemiology

AAION occurs almost exclusively in patients over the age of 60 years, more often in women.

NAAION is the most common optic neuropathy in patients over 50 years of age with an estimated annual incidence in the United States of 2/3–10/2 per 100,000 populations. There is no gender predisposition. The mean age at onset ranges from 57 to 65 years. NAION usually occurs in disks that have no central cup and which are considered "disk at risk." Vasculopathic risk factors, mainly systemic hypertension, diabetes, and hyperlipidemia are common. Sleep apnea and nocturnal hypotension are possibly associated with NAION, but further research is needed to confirm this association. Another possible connection is with the use of phosphodiesterase inhibitors (such as sildenafil) because of their hypotensive effect; however, proof of causation is still lacking.

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Optic Tract

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Definition

The optic tract (OT) is the portion of the optic pathway that connects the optic chiasm to the

lateral geniculate body (LGB) (Cummings 2013). Each OT contains the ipsilateral uncrossed temporal nerve fibers and contralateral nasal crossed nerve fibers that originate from the axons of the retinal ganglion cells (Binder et al. 2010). The blood supply of the OT derives from the anterior choroidal and posterior communicating arteries (Kanski and Bowling 2013). Damage to the OT may cause a contralateral relative afferent pupillary defect (RAPD), contralateral homonymous hemianopsia, and band optic atrophy (Friedman and Kaiser 2007).

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Optic Tract Lesion

► Retrochiasmal Disorders

Optical Aberrations

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Definition

Deviations from a diffraction-limited optical system causing deterioration of the optical image. Aberrations can be divided into chromatic (longitudinal) and monochromatic (wavefront) aberrations.

Basic Characteristics

An ideal optical system unites rays emerging from an object in a single point. Real optical systems like the human eye contain optical aberrations that cause a blur figure. *Chromatic* or *longitudinal aberration* is caused by the wavelength-dependence of dispersion of optical media. This results in different foci for different wavelengths. Chromatic aberration has effects also in the paraxial region and typically causes colored rims around objects. In contrast, *monochromatic* or *wavefront aberrations* are present if optical properties lead to different optical path lengths. Monochromatic aberrations vary with the angle of incidence of light rays and with the aperture diameter and cause an often asymmetric blur figure.

In physiological optics and ophthalmology, monochromatic aberrations play an important role. The human eye is afflicted mostly with defocus and astigmatism. The term *ametropia* applies, if the presence of defocus and astigmatism significantly affects the visual function of the uncorrected eye. While defocus causes a rotationally symmetric blur figure, astigmatism is characterized by different refraction along two orthogonal meridians. The resulting blur figure is cross-shaped and line-shaped if combined with defocus. Defocus and astigmatism can be corrected with glasses and are also referred to as *lower-order aberrations* (LOA). Correspondingly, *higher-order aberrations* (HOA) which cannot be corrected with conventional glasses exist. Presence of HOA causes an asymmetric blur figure, also if LOA are corrected with a sphero-cylindrical lens combination. The two most significant HOA are *coma* and *spherical aberration*. Coma describes an asymmetry of refraction along an axis through the middle of the pupil while spherical aberration is a rotational symmetric aberration characterized by difference of refraction from pupil center to the periphery. Other HOA are trefoil and other astigmatisms of higher frequency. In physiological optics, the polynomial expansion introduced by Zernike is typically used for description and quantification of the monochromatic aberrations of the eye (Thibos et al. 2002a). The Zernike expansion

allows an approximation and hence a reproducible quantification of the wavefront and its deviation from ideal optics (wavefront error). From the coefficients of the Zernike expansion, the optical transfer function and the point spread function can be calculated using Fourier transforms.

The normal human eye possesses both LOA and HOA in a characteristic pattern with rather insignificant contribution of HOA (Thibos et al. 2002b; Salmon and van de Pol 2006). In pathological conditions (keratoconus, cataract, corneal scars), HOA can reach high levels which affect visual function (Applegate et al. 2000; Fujikado et al. 2004). In clinical and laboratory settings, monochromatic aberrations of the eye are measured with aberrometers (Hartmann-Shack sensor, ray tracing, dynamic retinoscopy).

Cross-References

- ▶ Aberrometry
- ▶ Ametropia: Definition
- ▶ Comatic Aberrations
- ▶ Zernike Coefficients

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Optical Biometry

- ▶ Partial Coherence Interferometry

Optical Coherence Tomography

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Definition

Optical coherence tomography (OCT) is a non-contact optical imaging technology that allows high-resolution cross-sectional imaging of an object.

Purpose

Based on low-coherence interferometry, interference of light is shortened to a distance of µm, thus enabling "optical biopsy" (Drexler and Fujimoto 2008).

Principle

Time-domain OCT uses a scanning laser interferometer and an 820-nm infrared light source which is split into two separate beams. One of these beams scans the object of interest, whereas the other one serves as a reference beam which is reflected by a reference mirror. The distance of the reference mirror can be adapted and thus the time it takes for the reference beam to reach the sensor may be modified.

By comparing these two light beams, the backscattered light is measured and by this a cross-sectional image of the tested object is generated. The axial resolution of OCT is determined by the coherence length of the light, hence the name optical coherence tomography (Drexler and Fujimoto 2008).

A more recent development, spectral-domain OCT, also known as Fourier-domain OCT, allows retinal imaging at a scan speed 100 times faster and at a resolution up to five times higher than

TD-OCT. It is an imaging technique that makes use of the Fourier transformation to gather depth data from the spectra of the OCT signal. Hereby, the formerly required axial translation of the reference mirror to obtain depth information can be waived (Huang et al. 2008).

Indication

Imaging of anterior and posterior segments of the eye.

Contraindication

None.

Advantage/Disadvantage

Noncontact, real-time, in situ visualization of the internal microstructure of biological tissue, without the need to remove and process specimens.

Cross-References

- ▶ Anterior Chamber
- ▶ Anterior Segment Partial Coherence Interferometry
- ▶ Anterior Segment Surgery
- ▶ Biomicroscopy, Ultrasound, of Anterior Segment
- ▶ Choroidal and/or Ciliary Body and/or Iris Melanoma

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Optical Quality

▶ Image Quality, General

Optokinetic Nystagmus

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Synonyms

Optokinetic reflex

Definition

Optokinetic nystagmus (OKN) is a rhythmic involuntary conjugate ocular oscillation provoked by a compelling full visual field stimulus that is characterized by a set of alternating slow pursuit movement followed by a set of alternating slow (compensatory) and corrective fast (saccadic) phase of movement where the quick saccade brings the eyes back to the primary position once the eyes approach the limit of their rotation (Lavin 2012; May and Corbett 2013). The slow phases are in direction of the stimulation (Lavin 2012). As the head moves and a visual scene moves

across the retina (retinal slip) the eyes automatically compensate to stabilize the image on the retina, by undergoing optokinetic nystagmus (May and Corbett 2013).

The reflex begins with afferents from the wide-field retinal ganglion cells sensitive to slow movements of the whole receptive fields that are turned to directions comparable to the orientations of the vestibular semicircular canals (May and Corbett 2013). Retinal ganglion cells terminate in small nuclei along the incoming optic tract, composing the accessory optic system (AOS) (May and Corbett 2013). The AOS also receives input from the visual association cortex and projects to the nucleus reticularis tegmenti pontis and the inferior olive that supply the vestibulocerebellum and vestibular nuclei (May and Corbett 2013). Optokinetic neurons from the vestibular nuclei influence extraocular motor neurons and are required for a functional optokinetic reflex (May and Corbett 2013). The OKN reflex can be evoked by turning the patient in a revolving chair or using bedside optokinetic tape or an OKN drum. OKN testing can be used to evaluate foveal pursuit and refixation saccades in the circumstance of subtle internuclear ophthalmoplegia, provocation of convergence-retraction nystagmus, congenital nystagmus, psychogenic blindness or ophthalmoplegia, or homonymous hemianopia caused by a parieto-temporo-occipital lesion (Lavin 2012; Hullar et al. 2015).

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Optokinetic Reflex

► Optokinetic Nystagmus

Ora Serrata

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Synonyms

Peripheral retina

Definition

The ora serrata is the serrated anterior border of the neurosensory retina. It's dentate or "teeth-like" processes extend anteriorly into the pars plana of the ciliary body. Anatomically, it is located approximately 5–6 mm posterior to the limbus. Ora bays are created by extensions of the pars plana into the ora serrata, creating scalloped-shape borders.

Cross-References

► Ciliary Body
► Pars Plana; Pars Plicata
► Retina, Structure of

Orbit, Inflammation of

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See ► Orbital Cellulitis

Orbital Apex Syndrome in Neuro-Ophthalmology

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Definition

An orbital apex syndrome (OAS) is clinically defined by a combination of the involvement of orbital apex structures (e.g., orbital tissues, fat, and extraocular muscles) and several cranial nerves (i.e., oculomotor nerve (III), trochlear nerve (IV), abducens nerve (VI), trigeminal nerve (V1 branch)) and the optic nerve (II). There may be concomitant proptosis or other anterior orbital signs such as chemosis, proptosis, or periorbital edema and erythema from involvement of adjacent orbital tissues.

Etiology

OAS may be caused by inflammatory, infiltrative, infectious, neoplastic, iatrogenic, traumatic, or vascular processes. Typically iatrogenic/surgical, neoplastic, and inflammatory are the most common causes followed by vascular, infections, and other etiologies.

Inflammatory OAS

Inflammatory OAS may be idiopathic (idiopathic orbital inflammatory syndrome (IOIS)) or secondary to underlying systemic inflammation (e.g., granulomatosis with polyangiitis (formerly Wegener granulomatosis)), sarcoidosis, systemic lupus erythematosus, polyarteritis nodosa, and eosinophilic granulomatosis with polyangiitis (formerly Churg–Strauss syndrome). Typical inflammatory OAS occurs acutely with ipsilateral pain, ophthalmoplegia, and optic neuropathy. Steroids are the first-line therapy in presumptive IOIS but may be used for secondary OIS as well.

Infectious

Infectious diseases involving the central nervous system, paranasal sinuses, and periorbital structures may cause adjacent OAS. These can include fungal (e.g., mucormycosis and *Aspergillus*), bacterial (e.g., syphilis, bacterial orbital cellulitis, tuberculosis), viral (e.g., herpes zoster virus), or rarely parasitic disease. Mucormycosis should be suspected in individuals with a compromised immune system (e.g., diabetes mellitus (especially in diabetic ketoacidosis)), alcoholism, hematologic malignancies, solid organ (e.g., renal, lung, cardiac transplant) or bone marrow transplant survivors, and chronic immunosuppression (e.g., steroids or chemotherapy). These infectious etiologies for OAS can mimic the presentation of OIS and may present with ipsilateral pain, ophthalmoplegia, proptosis, and evidence for local tissue invasion. Thus, infectious etiologies should be excluded before starting corticosteroid therapy for presumed OAS due to OIS. Some fungal organisms are angioinvasive and can produce secondary tissue necrosis (i.e., "the black eschar"), but while distinctive this sign of necrosis is a late finding and often portends a negative prognosis. Bacterial orbital cellulitis is also a relatively common infectious cause of OAS (especially with concomitant adjacent sinusitis) and can be due to *Staphylococcus aureus*,

Streptococcus pneumoniae, other streptococci, gram-negative bacilli, and anaerobic bacteria.

Neoplastic

Neoplasms should be included in the differential of OAS. Primary ocular or orbital tumors, neoplasms of the paranasal sinuses, or central nervous system tumors may secondarily invade the orbital apex. These neoplasms include nasopharyngeal cancer, lymphoma, meningioma, and metastatic disease (breast, lung, kidney, and malignant melanoma). Typically, neoplastic etiologies for OAS produce slowly progressive, painless ophthalmoplegia and optic neuropathy, but some lesions (e.g., lymphoma or metastasis) may present acutely and mimic infectious or inflammatory presentations of OAS.

Iatrogenic/Traumatic

OAS has been reported with the following sinonasal and periorbital procedures: ethmoidal artery ligation, intranasal ethmoidectomy, and septorhinoplasty. OAS has also been observed after penetrating or blunt orbital trauma, usually accompanied by bone fracture.

Vascular

Vascular etiologies of OAS include cavernous carotid aneurysm, carotid–cavernous fistulas, and cavernous sinus thrombosis.

Table 1 summarizes the common etiologies for OAS.

Orbital Apex Syndrome in Neuro-Ophthalmology, Table 1 Common etiologies for OAS

Inflammatory
1. Sarcoidosis
2. Systemic lupus erythematosus
3. Eosinophilic granulomatosis with polyangiitis (Churg–Strauss syndrome)
4. Granulomatosis with polyangiitis (Wegener granulomatosis)
5. Idiopathic granulomatous cavernous sinus syndrome (Tolosa–Hunt syndrome)
6. Giant cell arteritis (orbital ischemia)
7. Idiopathic orbital inflammatory syndrome (i.e., orbital inflammatory pseudotumor)
8. Thyroid eye disease (TED)
Infectious
1. Fungi: Aspergillosis, mucormycosis
2. Bacteria: *Streptococcus* spp., *Staphylococcus* spp., *Actinomyces* spp., gram-negative bacilli, anaerobes, *Mycobacterium tuberculosis*
3. Spirochetes: *Treponema pallidum*
4. Viruses: Herpes zoster
Neoplastic
1. Head and neck tumors: nasopharyngeal carcinoma, adenoid cystic carcinoma, squamous cell carcinoma
2. Neural or nerve sheath tumors: neurofibroma, meningioma, ciliary neurinoma, schwannoma
3. Metastatic lesions: lung, breast, renal cell, malignant melanoma
4. Hematologic: Burkitt lymphoma, non-Hodgkin lymphoma, leukemia
5. Perineural invasion of cutaneous malignancy
Iatrogenic/traumatic
A. Iatrogenic
1. Sinonasal surgery
2. Orbital/facial surgery
B. Traumatic
1. Penetrating injury
2. Nonpenetrating injury
3. Orbital apex fracture
4. Retained foreign body
Vascular
1. Carotid cavernous aneurysm
2. Carotid cavernous fistula
3. Cavernous sinus thrombosis
4. Sickle cell anemia (orbital ischemia)
5. Giant cell arteritis
Others
Mucocele

Clinical Presentation

The most common initial symptoms of OAS are visual dysfunction due to optic neuropathy with variable partial or complete ophthalmoplegia with or without lid and pupil involvement. Optic nerve dysfunction can be documented by loss of vision, a relative afferent pupillary defect, loss of color vision or visual field, and optic disc edema or optic atrophy. Optic atrophy usually takes several weeks to months to develop and the disc may appear normal at onset (i.e., retrobulbar optic

neuropathy). Diplopia is also a common symptom in OAS but may be absent in cases with severe visual loss who are unable to appreciate diplopia or in cases of complete ptosis. Since multiple cranial nerves or extraocular muscles are usually affected in OAS, any degree of ophthalmoplegia from single or a combination of ocular motor cranial nerve palsies may occur.

Proptosis is present in up to 72% of OAS patients and depends on the degree of anterior orbital involvement. Smaller lesions in the orbital apex however may not have any appreciable proptosis and some orbital etiologies producing an OAS might produce enophthalmos (e.g., scirrhous breast carcinoma). Periorbital pain is also a common symptom in OAS. It is present in up to 50% of patients and may be seen secondary to generalized orbital inflammation or edema or be neurogenic in the distribution of the ipsilateral ophthalmic V1 nerve. Numbness or paresthesias may also occur in the trigeminal (V1) distribution. Some etiologies (e.g., adenoid cystic carcinoma, squamous cell carcinoma) may have a predilection for perineural involvement and are often painful. The absence of pain however does not exclude the diagnosis of OAS.

Diagnostics

Neuroimaging should be performed in all suspected OAS patients. Computed tomography (CT) of the orbit and head is the faster option. CT also plays an important role in the evaluation of patients who cannot have an MRI, for evaluation of sinus disease, bone, sinus disease, trauma patients, and those with suspected metallic foreign bodies. It is important to remember that CT is superior to MRI in evaluation or bony anatomy. MRI of the brain and orbit (with fat suppression) with and without contrast is superior for showing soft tissue involvement and intracranial extension. If a vascular lesion is suspected, MRA (or CTA) could also be included but has variable sensitivity. Thus, even if the MRA/CTA is negative but the clinical suspicion remains high, then a standard catheter angiography should still be considered.

Depending on the clinical suspicion, laboratory tests for suspected inflammatory or infectious etiology might include erythrocyte sedimentation rate and C-reactive protein (especially in elderly patients suspected of harboring giant cell arteritis), complete blood count, syphilis serology (e.g., rapid plasma regain (RPR), microhemagglutination assay for *Treponema pallidum (MHA-TP)*), angiotensin-converting enzyme, perinuclear antineutrophil cytoplasmic antibody (p-ANCA), cytoplasmic antineutrophil cytoplasmic antibody (c-ANCA), antinuclear antibody (AMA), purified protein derivative (PPD), and HIV testing. Chest radiography or chest CT scan (for sarcoid and granulomatosis with polyangiitis) and lumber puncture could also be considered depending on the clinical presentation.

Differential Diagnosis

Differential Diagnosis includes:

- Cavernous sinus syndrome (without optic neuropathy)
- Superior orbital fissure syndrome (with optic neuropathy)

Prophylaxis

Non-applicable.

Therapy

The management of OAS depends on the underlying etiology. Corticosteroids are usually indicated in inflammatory cases. Infectious etiologies require antibiotic therapy, and often broad spectrum antibiotic therapy is deployed until the results of gram staining and cultures are

known. Fungal disease (mucormycosis) especially in diabetic ketoacidosis or other immunosuppressed patients should be ruled out before corticosteroids are started, and in general, antifungal therapy requires a confirmatory fungal biopsy or culture. Methotrexate, azathioprine, and radiotherapy have all been used in inflammatory disease resistant to steroids. Neoplastic lesions typically require biopsy confirmation and treatment depends on the underlying histopathology.

Prognosis

The prognosis varies according to etiology. In general infectious and inflammatory conditions (except *Mucor*) respond to early and aggressive treatment with up to 75% of patients experiencing some improvement. Neoplastic and vascular etiologies have variable prognosis.

Epidemiology

OAS may affect any age, either gender, and any race. Some neoplastic conditions are more common in children (e.g., neuroblastoma, rhabdomyosarcoma, optic glioma) or in adults (e.g., meningioma). The etiologies of orbital cellulitis also might vary according to age.

Cross-References

► Cavernous Sinus Syndrome
► Superior Orbital Fissure

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Orbital Cellulitis

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Synonyms

Abscesses, orbital; Orbit, inflammation of

Definition

Orbital cellulitis is a sight-threatening and potentially life-threatening infection of the orbital fat, muscles, and/or bones posterior to the orbital septum more common in young children than adults. Inflammation within the orbit may affect the orbital tissues (resulting in chemosis and proptosis), extraocular muscles (resulting in dysmotility and diplopia), and/or the optic nerve at the orbital apex (resulting in decreased visual acuity and an afferent pupillary defect). It must be distinguished from preseptal cellulitis (inflammation anterior to the orbital septum) as mortality, risk of vision loss, and other complications are higher with orbital cellulitis than preseptal cellulitis (Garcia and Harris 2000).

Etiology

Orbital cellulitis commonly occurs secondary to direct extension from an ipsilateral sinus infection – especially the ethmoid sinus, which is separated from the orbit only by the thin lamina papyracea (Osguthorpe and Hochman 1993).

Other risk factors for orbital cellulitis include ophthalmic or sinus surgery, trauma, infected mucocele, and areas of infection in close proximity (face, teeth, middle ear, lacrimal system, globe).

Historically, *Staphylococcus aureus*, *Streptococcus* species, *Haemophilus* species, and anaerobes have been the most commonly reported organisms in culture-positive cases. However, since the implementation of vaccination against *Haemophilus influenzae* type B in the USA, this particular pathogen has been rarely reported (Ambati et al. 2000). Antibiotic-resistant strains of bacteria, particularly methicillin-resistant *Staphylococcus aureus* (MRSA), are increasingly encountered and may be more likely to present in an atypical location in the orbit and extend intracranially (McKinley et al. 2007). Mycobacteria, *Bacillus* species, fungi, and *Pseudomonas* are less common isolates. Diabetics and immunocompromised patients are predisposed to *Mucor*/zygomycosis.

Epidemiology

Orbital cellulitis is more common in children than adults. There is an associated mortality of 1–2% and a risk vision loss of up to 11%; such complications are extremely rare in preseptal cellulitis. In a retrospective case series of 315 children admitted to a hospital with preseptal or orbital cellulitis, 18 patients were diagnosed with orbital cellulitis and all of these had a history of sinusitis. The incidence of sinusitis in the remaining 297 patients with preseptal cellulitis was only 14.5% (Osguthorpe and Hochman 1993).

Clinical Presentation

Orbital cellulitis may be clinically indistinguishable from preseptal cellulitis, periosteal abscess, and orbital abscess but should be suspected in any patient presenting with chemosis, elevated intraocular pressure, globe displacement, pain with eye movement, motility defects, and change in vision, especially if the history is suggestive of recent febrile upper respiratory or sinus infection. A complete eye examination is indicated for evaluation of disease severity and to exclude other causes of proptosis with decreased vision (namely, retinoblastoma, rhabdomyosarcoma, and orbital inflammatory syndrome).

Preseptal cellulitis more commonly arises from contiguous infection from the upper face or local trauma, is rarely associated with sinusitis, and is less likely to result in globe displacement, motility defects, or vision disturbance. Limitation of eye movement and vision loss in particular suggest orbital involvement.

Subperiosteal abscesses or orbital abscesses can be sequelae of orbital cellulitis, though subperiosteal abscesses are sometimes the first sign of extension of a sinus infection into the orbit and may rupture causing orbital cellulitis (McKinley et al. 2007).

Diagnostics

Clinical examination (especially visual acuity and motility) should be used to arrive at an initial diagnosis and guide treatment. Most clinicians also recommend CT imaging to evaluate the extent and severity of disease and rule out less common entities (i.e., orbital inflammatory syndrome, Wegener's granulomatosis, posterior scleritis), though some feel that exposing a child to radiation is unnecessary if the clinical exam and history are consistent and the child responds well to an empiric antibiotic regimen.

Differential Diagnosis

Posterior scleritis
Tumors (retinoblastoma, rhabdomyosarcoma)
Wegener's granulomatosis
Idiopathic orbital inflammation
Tolosa-Hunt syndrome
Thyroid eye disease
Mucormycosis/zygomycosis
Severe allergic reaction

The differential for preseptal cellulitis includes: conjunctivitis, hordeolum, trauma, insect bites, and herpetic infections.

Treatment

If orbital cellulitis is suspected, expedient diagnostic imaging or surgical exploration may be required as timely intervention is necessary to prevent complications such as retinal artery occlusion and intracranial extension, which can result in meningitis, cavernous sinus thrombosis, or intracranial abscesses. Blood cultures are frequently negative and cultures from mucosal surfaces may show only normal flora. Cultures obtained by sinusotomy and orbitotomy have the highest yield (McKinley et al. 2007).

Broad-spectrum intravenous antibiotics and hospitalization with frequent bedside examinations are indicated in cases of orbital cellulitis and severe preseptal cellulitis. Initial antibiotic coverage should be guided by local epidemiologic data. Patients should be switched to other antibiotics, if indicated, based on culture sensitivities as they become available. In areas where the prevalence of MRSA is high, empiric coverage with parenteral vancomycin, clindamycin, and cefotaxime may be preferred and should be continued until the patient shows clinical improvement (including resolution of fevers and leukocytosis) and can be switched to an oral regimen.

Aggressive nasal hygiene with nasal corticosteroids, saline irrigation, and decongestants is indicated. Intravenous dexamethasone reduces inflammation, reduces the development of septations, and does not appear to increase the incidence of complications (Yen and Yen 2005). Serial CT imaging may be required to evaluate for subperiosteal/orbital abscess and efficacy of treatment, though imaging tends to lag behind clinical response (Harris 1996).

Orbital surgery is indicated if the organism cannot be isolated from other cultures or if the patient fails to respond to conservative measures, clinically deteriorates, or develops an abscess along the lateral, superior, or inferior orbital wall. Small medial subperiosteal abscesses may be drained endoscopically or managed medically (Garcia and Harris 2000). Drain placement following surgery reduces the risk of abscess formation. An interdisciplinary approach may be necessary for the management of complications such as persistent sinus infection, intracranial spread, or cavernous sinus thrombosis.

Mild preseptal cellulitis can be managed with oral antibiotics (such as amoxicillin and clavulanate) on an outpatient basis with close follow-up.

Prognosis

A patient's prognosis depends on many factors including age, disease extent and severity at the time of presentation, duration of symptoms, microorganism, and immunodeficiency status. With timely intervention, vision loss and death are rare.

Cross-References

- ▶ Retinoblastoma
- ▶ Rhabdomyosarcoma of Orbit

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Orbital Compartment Syndrome

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Synonyms

Increased orbital pressure; Orbital compression syndrome; Orbital tension syndrome

Definition

An acute elevation of intraorbital pressure resulting in damage to ocular and other intraorbital structures.

Etiology

The orbit is a confined space which follows a pressure-volume curve. The orbit may compensate for small increases in orbital volume by forward movement of the globe and orbital fat prolapse. However, once the intraorbital pressure rises beyond the orbit's capacity to compensate, there is a rapid rise in intraorbital tissue pressure. This increase in tissue pressure is associated with a decrease in perfusion of orbital tissues, including the optic nerve and globe. The most common cause of orbital compartment syndrome (OCS) is a retrobulbar hematoma as a result of trauma or surgery. Orbital infection, emphysema, tumor, or inflammation may also cause an increase in orbital pressure leading to a compartment syndrome. Other less common causes of OCS include large-volume resuscitation, traumatic asphyxia syndrome, extravasated contrast material, foreign body, spinal surgery in the prone position, spontaneous bleeding from orbital vascular anomalies or complications related to sclerotherapy for such disorders, and disseminated intravascular coagulation.

Clinical Presentation

Patients with orbital compartment syndrome often report an acute onset of eye pain and proptosis. They may also report vision loss, double vision, nausea, and vomiting. These symptoms may develop over a period of minutes to hours. The patient may have a history of recent trauma, surgery, sinusitis, or a bleeding disorder. On external examination, there is usually periorbital edema and ecchymosis, limited extraocular motility, and resistance to retropulsion. There may also be conjunctival chemosis and hemorrhage. Vision may be decreased, and there may also be an afferent pupillary defect and increased intraocular pressure. Fundus examination may reveal disk edema, choroidal folds, central retinal artery pulsations, and a central retinal artery occlusion with a cherry red spot.

Diagnosis

Diagnosis is often made in the context of a medical history and physical examination which are consistent with orbital compartment syndrome. A complete ophthalmic exam must be performed. Special attention should be given to looking for an afferent pupillary defect, loss of color vision, increased intraocular pressure, central retinal artery pulsations, disk edema, and choroidal folds. Computed tomography (CT) or magnetic resonance imaging (MRI) of the orbit may help to elucidate the cause of the compartment syndrome; however, OCS is a clinical diagnosis, and therapeutic intervention should not be delayed to obtain imaging.

Differential Diagnosis

The differential diagnosis for orbital compartment syndrome includes autoimmune orbital inflammation, thyroid eye disease, ruptured dermoid cyst, progressively enlarging orbital masses, orbital fractures, and traumatic optic neuropathy.

Prophylaxis

The use of restraints, seat belts, and protective headgear can help prevent orbital compartment syndrome caused by trauma.

To minimize the risk of orbital hematoma and OCS associated with orbital and periorbital surgery, the following measures should be taken:

1. Perioperative anticoagulants should be avoided, when possible.
2. During surgery, special attention should be given to achieving hemostasis and avoiding large blood pressure fluctuations.
3. Awakening from general anesthesia should be performed with adequate pain and nausea control and suppression of the cough reflex to reduce straining and the risk of orbital hemorrhage.

Therapy

The presence of vision loss or an afferent pupillary defect in association with orbital compartment syndrome necessitates immediate therapy with soft tissue decompression of the orbit by lateral canthotomy and cantholysis. If OCS is suspected, decompression should not be delayed to obtain confirmatory imaging. To release the lateral canthus, first inject a local anesthetic in the region of the lateral commissure. Next, clamp a hemostat horizontally at the lateral canthus for 60 s to compress the tissues and reduce bleeding. The clamp is then released, and a scissor is used to create a horizontal incision of approximately 1 cm into the compressed tissue. Then the inferior crus of the lateral canthal tendon is located and lysed. Successful release of the inferior crus will allow the eyelid to easily evert and the globe to sublux forward. This subluxation is beneficial, as it releases intraorbital pressure on the optic nerve. If releasing the inferior crus of the lateral canthal tendon does not provide the desired amount of decompression, the superior crus of the lateral canthal tendon may also be severed in a similar fashion. Finally, a bony orbital decompression may be required in extreme cases of OCS which do not adequately respond to soft tissue decompression.

Additionally, the following medical treatments may be instituted concurrently with surgical treatment of OCS, assuming no contraindications:

1. Oral carbonic anhydrase inhibitor (e.g., acetazolamide)
2. Topical beta-blocker, alpha-agonist, or topical carbonic anhydrase inhibitor
3. Hyperosmotic agent (e.g., mannitol)

Prognosis

The amount of time elapsed until treatment of orbital compartment syndrome appears to be the most significant factor in predicting visual outcome. Prompt treatment of orbital compartment syndrome with orbital decompression and medical management is much more likely to result in visual recovery. Several studies show that delayed treatment is more likely to result in permanent vision loss. Younger patients are also more likely to recover vision after treatment of OCS.

Epidemiology

Orbital compartment syndrome is a rare complication of facial trauma or surgery. The exact incidence is unknown. Orbital hemorrhage from a variety of causes accounts for the majority of orbital compartment syndrome cases. The incidence of orbital hemorrhage after blepharoplasty is 0.055% (1/2000) and that with permanent visual loss is 0.0045% (1/10,000). Orbital hemorrhage has an incidence of approximately 1% from retrobulbar and peribulbar anesthetic injections, and it is also the most frequent ophthalmic complication of endoscopic sinus surgery, with an incidence of 0.12%.

Cross-References

- ▶ Abscesses, Orbital
- ▶ Canthal Reconstruction
- ▶ Globe, Displacement of, in Orbital Disorders
- ▶ Intraorbital Foreign Body (IOFB)
- ▶ Orbit, Inflammation of
- ▶ Orbital Cellulitis
- ▶ Orbital Hemorrhages
- ▶ Orbital Pain
- ▶ Three-Dimensional Computed Tomography, in Orbital Evaluation
- ▶ Tight Orbit

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Orbital Compression Syndrome

- ▶ Orbital Compartment Syndrome
- ▶ Orbital Hemorrhages

Orbital Floor Fracture

- ▶ Blowout Fractures

Orbital Hemorrhages

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Synonyms

Orbital compartment syndrome; Orbital compression syndrome; Orbital tension syndrome; Retrobulbar hemorrhage

Definition

Hemorrhage within the orbital space.

Etiology

Orbital hemorrhage usually occurs in the setting of trauma or secondary to periocular or intraocular surgery with retrobulbar anesthesia. Spontaneous hemorrhage can occur from valsalva maneuvers, coughing, sneezing, exertion, or bleeding from an orbital vascular tumor or malformation.

Clinical Presentation

Patients with retrobulbar hemorrhages present with the acute onset of pain, pressure, vision change, diplopia, nausea, or vomiting, usually in the setting of trauma or recent periocular or intraocular surgery. The most common presenting signs are: decreased visual acuity, extraocular muscle limitation, periocular ecchymoses, subconjunctival hemorrhagic chemosis, pupillary abnormalities, increased resistance to retropulsion, increased intraocular pressure, and dyschromatopsia.

Diagnosis

Diagnosis is made clinically by evaluating for the typical signs and symptoms of orbital hemorrhages. Diagnosis can be confirmed by orbital imaging, but imaging is not necessary and should not delay potential treatment of an orbital hemorrhage in the acute setting of threat to vision.

Differential Diagnosis

The differential diagnosis of an orbital hemorrhage includes an orbital hematoma, orbital cellulitis, orbital inflammation, an orbital mass, ruptured dermoid cyst, orbital vascular tumors and malformations, and orbital fractures (Ehlers et al. 2008).

Prophylaxis

The use of restraints, seat belts, and protective headgear can help prevent orbital hemorrhage caused by trauma.

To minimize the risk of orbital bleeding associated with periocular and intraocular surgery, the following measures should be taken (Hass et al. 2004):

1. Perioperative anticoagulants should be avoided, when possible.
2. During surgery, special attention should be given to achieving hemostasis and avoiding large blood pressure fluctuations.
3. Awakening from general anesthesia should be performed with adequate pain and nausea control and suppression of the cough reflex to reduce straining.

Therapy

In the setting of progressive orbital signs and/or vision loss, treatment should be instituted emergently (see Table 1).

Assuming no contraindications, medical treatment options include the use of intravenous steroids and therapies aimed at decreasing the intraocular pressure such as:

1. Oral carbonic anhydrase inhibitor (e.g., acetazolamide)
2. Topical beta-blocker, alpha-agonist, or topical carbonic anhydrase inhibitor
3. Hyperosmotic agent (e.g., mannitol)

Surgical treatment in the setting of recent orbital or eyelid surgery may involve opening of the wound to evacuate hematoma and to search for and control the source of bleeding. In cases related to trauma or retrobulbar injections, a lateral canthotomy with inferior cantholysis should be performed. In refractory cases, the superior canthal tendon can also be disinserted. Rarely, persistent vision loss with posteriorly collecting hemorrhage may respond to orbital decompression surgery.

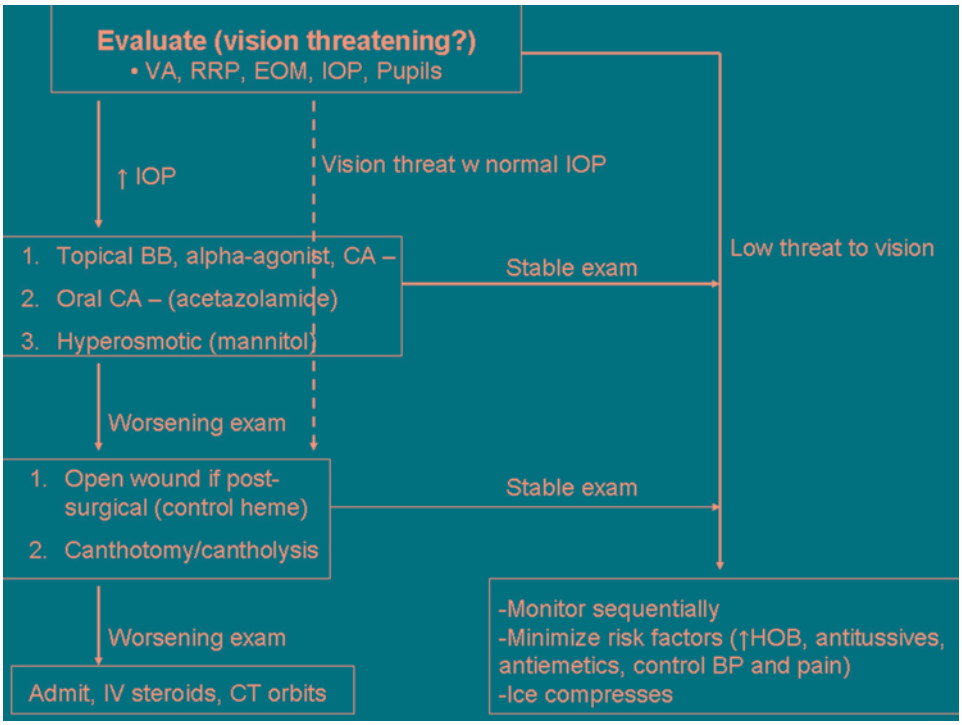
Prognosis

The amount of time elapsed until treatment of an orbital hemorrhage appears to be the most significant factor in predicting visual outcome. Prompt treatment of an orbital bleed is much more likely to result in visual recovery. Several studies show that delayed treatment is more likely to result in permanent vision loss.

Epidemiology

The incidence of orbital hemorrhage after blepharoplasty is 0.055% (1/2000) and subsequent permanent visual loss is 0.0045% (1/10,000). Orbital hemorrhage has an incidence of approximately 1% from retrobulbar and peribulbar anesthetic injections, and it is also the most frequent ophthalmic complication of endoscopic sinus surgery, with an incidence of 0.12%.

Orbital Hemorrhages, Table 1 Treatment algorithm for orbital hemorrhage



Cross-References

- ▶ Abscesses, Orbital
- ▶ Canthal Reconstruction
- ▶ Globe, Displacement of, in Orbital Disorders
- ▶ Orbit, Inflammation of
- ▶ Orbital Cellulitis
- ▶ Orbital Pain
- ▶ Three-Dimensional Computed Tomography, in Orbital Evaluation
- ▶ Tight Orbit

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Orbital Hypertelorism

- ▶ Telorbitism (Hypertelorism)

Orbital Pain

- ▶ Pulsation, Orbital

Orbital Tension Syndrome

- ▶ Orbital Compartment Syndrome
- ▶ Orbital Hemorrhages

Orbitotomy

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Definition

A surgical procedure to obtain access and exposure to a particular area of the orbit.

Indications

It is performed for multiple reasons, including biopsy or excision of a lesion, decompressing the optic nerve or canal, draining an abscess, removing a foreign body, and removing bone or fat for decompression of the orbit or for orbital fracture repair (Cockerham et al. 2001; Levine 2003; Nerad 2001).

Contraindication

Contraindication for patients unable to medically tolerate surgery.

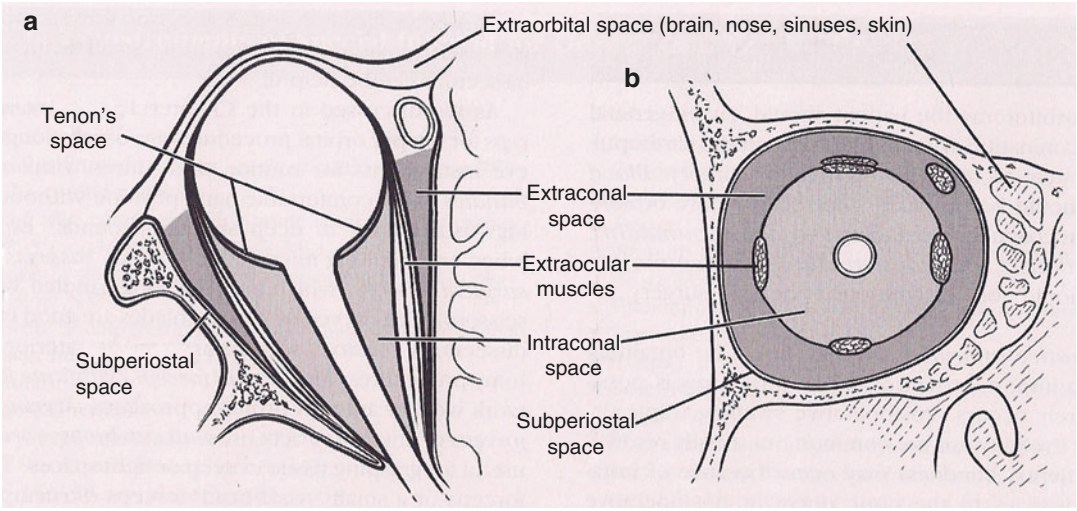
Techniques and Principles

An anterior orbitotomy is planned for a lesion in the anterior 2/3 of the orbit. A medial orbitotomy is useful for medial intra- and extraconal lesions, and a lateral orbitotomy is useful for lesions in the posterior orbit lateral to the optic nerve.

There are specifically defined surgical spaces in the orbit (Fig. 1)

1. The intraconal (central) space is the space between the muscle cone.
2. The extraconal (peripheral) space is the area between the periosteum and the muscle cone.
3. The subperiosteal, or extraperiosteal, space is the area beneath the peri-orbita or periosteum of the orbit.
4. The episcleral space is the area between Tenon's capsule and the globe.

The appropriate surgical approach is often determined by considering the location, type and size of lesion and surgical goals (biopsy vs. total excision) and is often driven by clinical findings as well as imaging studies. The most direct route should be used, keeping in mind normal anatomical structures in the orbit that may be nearby. Occasionally, help from other



Orbitotomy, Fig. 1 Surgical spaces of the orbit in coronal (**a**) and axial (**b**) view (Printed with permission from Nerad JA, ed. Oculoplastic Surgery. The requisites in ophthalmology. St. Louis: Mosby, Inc. 2001: 391)

specialists, such as neurosurgeons or otolaryngologists, is required to accomplish the goal and to provide alternative approaches to orbital spaces (Cockerham et al. 2001; Levine 2003; Nerad 2001).

Outcome

Access to the orbit for biopsy, excision, decompression, or fracture repair.

Complications

Risks of an orbitotomy include risks associated with anesthesia, bleeding, pain, infection, scarring, swelling, loss of vision, damage to adjacent structures, diplopia, and need for additional procedures.

Cross-References

- ▶ Anterior Orbitotomy
- ▶ Extraperiosteal Route
- ▶ Lateral Orbitotomy
- ▶ Orbit, Inflammation of

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Orbito-Zygomatico-Maxillary Fracture

- ▶ Zygomatic-Maxillary Complex Fractures

Organic Pigments

- ▶ Carotenoids (Xanthophylls)

Ornithine Aminotransferase (OAT) Deficiency

- ▶ Choroid, Gyrate Atrophy of

Oscillopsia

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Definition

Oscillopsia is a patient symptom of an illusory to-and-fro movement of a known stable environment and may be the result of ocular instability or impaired spatial constancy. These perceived environmental movements can be in any plane – vertical, horizontal, or torsional (Miller et al. 2008; Straube et al. 2012).

Etiology

Oscillopsia usually results from ocular instability or impaired spatial constancy. When oscillopsia is identified as a result of ocular instability, it can be characterized as constant or paroxysmal (Miller et al. 2008). Constant or permanent oscillopsia can be further divided into three deficiency areas: the fixation system, the visuo-vestibular stabilizing system, and the neural integrator (Miller et al. 2008; Tilikete and Vighetto 2011; Straube et al. 2012).

The fixation system, through visual and cerebellar feedback loops, allows for maintained gaze on a single point or object in space (Miller et al. 2008). Disruption of this control system can result in nystagmus (Straube et al. 2012). Acquired pendular nystagmus (nystagmus with back-to-back slow phases) stems from a variety of causes, most notably multiple sclerosis (MS) and oculopalatal tremor (OPT) (Tilikete and Vighetto 2011; Straube et al. 2012). MS is responsible for disrupting the visual/motor feedback loops resulting in the nystagmus, while OPT is involved with the cerebellar feedback loops likewise disrupting the fixation system (Tilikete and Vighetto 2011).

The visuo-vestibular stabilizing system allows one to maintain a stable gaze regardless of head/body movement with respect to the environment. The vestibulo-ocular reflex (VOR) induces ocular movements which compensate for these head movements, while the fixation system inhibits these movements in the case of tracking a moving object (Miller et al. 2008; Tilikete and Vighetto 2011). Disruption of this stabilizing system may manifest as a type of jerk nystagmus (fast and slow phases) resulting from cerebellar or brain stem dysfunction. Primary position downbeat nystagmus (PPDN) or primary position upbeat nystagmus (PPUN) may reveal disruption of the visuo-vestibular reflex, resulting in oscillopsia (Straube et al. 2012).

The neural integrator is responsible for extraocular muscle control during eccentric eye position (gaze away from the center of the eye). Disruption of this system, primarily the result of cerebellar or brain stem lesions, results in gaze-evoked nystagmus (eyes drifting back toward midline during eccentric gaze) (Miller et al. 2008; Tilikete and Vighetto 2011).

Spatial constancy is the culmination of anticipation and compensation of movements during focus on an object. Paroxysmal oscillopsia resulting from peripheral ocular motor or vestibular hyperactivity can also occur (Straube et al. 2012). Superior oblique myokymia results in episodes of monocular oscillopsia from trochlear nerve hyperactivity. Superior canal dehiscence syndrome may result in episodes of oscillopsia triggered by loud sounds (Tullio phenomenon) or other maneuvers which increase intracranial pressure (Miller et al. 2008; Tilikete and Vighetto 2011; Straube et al. 2012).

Treatment

Treatment should be directed at the underlying etiology of the oscillopsia (Tilikete and Vighetto 2011).

Prognosis

The recovery of oscillopsia is highly dependent on the underlying etiology (Miller et al. 2008; Tilikete and Vighetto 2011).

Cross-References

▶ Nystagmus

References

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Osler-Weber-Rendu Syndrome

▶ Hereditary Hemorrhagic Telangiectasia (Osler-Weber-Rendu Disease)

Osseous Choristoma

▶ Choroidal Osteoma

Osteogenesis Imperfecta, Blue Sclera

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Definition

The sclera is composed of type I collagen and is not blue in color; rather, this term refers to its blue-gray appearance due to thinning that reveals the uveal color underneath.

Etiology

Thinning of the sclera due to mutations in COL1A1 and COL1A2 reveal the underlying blood and uveal pigment. Abnormalities in type I collagen fibers reduce their diameter and affect their cross-striation, thus generating a more translucent collagen (Rajendran 2009). This allows visualization of the underlying uvea which appears blue.

Occurrence

Blue sclera that persists throughout life is a feature of type I osteogenesis imperfecta. Osteogenesis imperfecta type II is a lethal perinatal form that also causes a blue sclera sign. Patients with type III-IV may initially present with a light blue sclera that resolves by adulthood (Traboulsi 2006).

Osteogenesis Imperfecta, Blue Sclera, Table 1 Clinical findings in OI

Type of osteogenesis imperfecta	Clinical findings
OI – I (nondeforming OI with blue sclera)	Blue sclera. Hearing loss in 50% of patients
OI – II (perinatally lethal OI)	Dark blue sclera. 90% dies before 4 weeks of age. In utero fractures in 100% of patients
OI – III (progressively deforming OI)	Sclera may be blue at birth, but gradually normalizes with age. Progressive deformity of the skeleton
OI – IV (common variable OI with normal sclera)	Normal sclera. A blue tinge might be seen at birth in some cases and normalizes in childhood
OI – V (OI with calcification in interosseous membranes)	Normal sclera. Calcification of interosseous membranes in forearm in childhood leading to problems with pronation and supination

Classification

Although blue sclera is most frequently associated with osteogenesis imperfecta type I, other types may demonstrate subtle findings, as evidenced in Table 1.

Blue Sclera associated with osteogenesis imperfecta is a chronic and long-standing sign, in contrast to acute thinning of sclera which can be associated with systemic and/or inflammatory conditions (Van Dijk and Sillence 2014).

Cross-References

▶ Blue Sclera
▶ Connective Tissue Disease
▶ Cornea Plana
▶ Ehlers-Danlos Syndrome, Gene Linkage of Disease

- ▶ Melanosis
- ▶ Oculomandibulofacial Dyscephaly (Hallermann-Streiff Syndrome)
- ▶ Staphylomas, Congenital, Anterior

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Other Uveitic Etiologies

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Synonyms

Inflammatory eye disease; Secondary glaucoma in uveitis; Uveitic glaucoma

Definition

Intraocular pressure (IOP) rises due to intraocular inflammation, which may lead to optic nerve damage.

Etiology

Mostly infectious but also some noninfectious uveitis entities that can lead to a secondary IOP rise. A direct obstruction of the trabecular meshwork or trabeculitis is thought to be responsible (Radhakrishnan et al. 2010). This has to be distinguished from secondary glaucoma caused by complications of long-standing uveitis.

The prevalence of secondary glaucoma increases with chronicity and severity of disease.

- Infectious: herpetic anterior uveitis (HSV, VZV, and CMV) is the leading entity, but also other infectious uveitis forms as, e.g., toxoplasmic chorioretinitis, syphilis, or tuberculosis, can be accompanied by anterior chamber reaction and subsequent pressure rise.
- Noninfectious: the most typical is sarcoidosis-associated anterior uveitis or panuveitis.

Clinical Presentation

Patients with infectious uveitis present with unilateral uveitis of sudden onset and most often granulomatous keratic precipitates (KP). In the case of herpetic origin, segmental or patchy iris atrophy can be seen and often corneal involvement in the form of endotheliitis and/or corneal edema (Filho and Liesegang 2010a; b).

Patients with noninfectious uveitis and elevated IOP more frequently show bilateral disease. Granulomatous KP and Koeppe or Busacca nodules are a hallmark of sarcoidosis-associated uveitis.

Diagnosis

Tonometry should be performed in all uveitis patients at presentation. Return of ciliary body function with subsidence of uveitis may be associated with a rise in IOP. Therefore, it is important to continue monitoring IOP long enough as the inflammation resolves. Where herpetic uveitis is suspected, corneal sensitivity testing before administering local anesthesia should be performed. Gonioscopy is obligatory to find out the pathogenesis (open angle or angle closure) of IOP elevation.

Friederike Mackensen: deceased.

Differential Diagnosis

Entities, where noninflammatory material blocks the trabecular pores, as lens material in phacolytic glaucoma, red blood cells in hyphema, or photoreceptor segments in retinal detachment (Schwartz-Matsuo syndrome).

Prophylaxis

Antiherpetic therapy should be given for an appropriate length of time; sometimes many years of low-dose therapy are needed. Low-dose corticosteroid drops should be given in all cases, e.g., 1–2 drops of prednisolone acetate 1% daily. Visual field examination and structural measurements of the optic nerve head and RNFL should be repeated in regular intervals.

Therapy

IOP normalizes with control of inflammation. Thus, infectious uveitis has to be treated according to the pathogen involved, adding local and sometimes oral corticosteroids. Noninfectious uveitis should be treated with local and/or oral corticosteroids. Sometimes it will be difficult, especially in noninfectious uveitis, to distinguish secondary glaucoma caused by inflammatory activity or scarring from corticosteroid-induced IOP raise. Gonioscopy should be performed, and if in doubt local treatment may be changed to oral corticosteroids or to loteprednol with lesser probability of causing an IOP rise. Only few patients where complications as anterior synechia have taken place will require continued antiglaucomatous treatment or surgery.

Prognosis

Prognosis is generally good, but it depends on the time of inflammation, equalling the likelihood of complications having taken place. Relapsing herpetic anterior uveitis that is not properly treated will lead to optic nerve damage as well as scarring of the trabecular meshwork, so pressure control in some cases may only be achieved by surgical methods.

Epidemiology

IOP rise is observed in about 20% of uveitis patients, but only 35% of them had glaucoma (Sallam et al. 2009). In herpetic anterior uveitis, HSV is found more frequently than VZV, and patients with HSV-associated uveitis seem to be younger than those where VZV is involved (Van der Lelij et al. 2000). Still manifest secondary glaucoma is a rare complication in only 2–4% of cases (Tugal-Tutkun et al. 2010).

Cross-References

- ▶ Fuchs' Uveitis Syndrome (FUS) with Secondary Glaucoma
- ▶ Posner-Schlossman Syndrome
- ▶ Uveitic Glaucoma

References

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Overriding Orbicularis

► Botox: Spastic Entropion

Oxyphile Cell Adenoma

► Oncocytoma

Oxyphilic Cystadenoma

► Oncocytoma

P

Pachometry

► Pachymetry (Pachometry)

Pachy (for Short)

► Pachymetry (Pachometry)

Pachymetry (Pachometry)

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Synonyms

Pachometry; Pachy (for short)

Definition

Measurement of the thickness of the cornea, by means of a pachymeter.

Purpose

To measure the thickness of the cornea.

Principle

An instrument used for this purpose is called a pachymeter. Earlier forms of pachymetry are based on optical methods, while modern ones are based on ultrasound methods. Some methods require contact with the cornea, whereas others do not. A conventional pachymeter uses an ultrasonic transducer that touches the cornea and displays the thickness of the cornea, usually in micrometers, at the point of contact. By knowing the speed of sound through corneal tissue and the time it takes for the sound to travel through the cornea, one can calculate the thickness of the cornea. Other methods include confocal microscopy, optical coherence tomography (OCT), scheimpflug, and corneal waveform. OCT can provide a thickness map of the entire cornea.

Indication

It is useful in the screening and management of diseases such as glaucoma, Fuch's corneal dystrophy, and keratoconus and is pertinent for the planning of refractive surgery. Average corneal

U. Schmidt-Erfurth, T. Kohnen (eds.), *Encyclopedia of Ophthalmology*,
https://doi.org/10.1007/978-3-540-69000-9

thickness is approximately 530–545 μm in non-glaucomatous eyes.

Contraindication

There are no contraindications per se as pachymetry is noninvasive. However, some methods require corneal contact with the probe of the pachymeter.

Reference

External Disease and Cornea (2011) Basic and clinical science course, section 8. AAO, p 28

Palinopsia

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Synonyms

Afterimages; Visual perseveration

Definition

Palinopsia is a visual disturbance where images persist after their corresponding environmental stimulus is no longer present (Bender et al. 1968). Typically palinopsia is categorized into two different subgroups, illusory and hallucinatory. Illusory palinopsia consists of prolonged indistinct afterimages, light streaking, visual trailing, and momentarily formed image perseveration (Gersztenkorn and Lee 2014). Hallucinatory palinopsia consists of formed image perseveration, scene perseveration, categorical incorporation (a patient seeing an object or feature and then superimposing it onto comparable objects or people), and patterned visual spread (Gersztenkorn and Lee 2014).

Etiology

Palinopsia has many different etiologies. Some of these etiologies include: post-geniculate cortical lesions, metabolic or systemic disease, idiopathic seizures, diffuse cortical pathology, drug induced, migraine, head trauma, psychiatric conditions, and visual snow clinical syndrome (Gersztenkorn and Lee 2014).

Clinical Presentation

Palinopsia is a constellation of symptoms that are ascertained by a detailed medical history. The physician will need to determine if the afterimages are best described as a hallucinatory or illusory palinopsia. Some key indicators include: content, duration, and quality (e.g., color, shape, motion) of the persisting images or scenes. The episodes may vary by time of day, the number and frequency of episodes, and the location in the visual field of the original and perseverated images. Sometimes light or motion exacerbates or precipitates the palinopsia (Abert and Ilsen 2010). It is important to obtain a careful neurological history of migraines, cerebrovascular accidents, seizure disorder, or neoplasm because these disorders can all cause palinopsia. The examiner should

also ask about prescription drug use, head trauma, and hallucinogenic drug use (Abert and Ilsen 2010).

Diagnostics

Visual fields and neuroimaging should be obtained in patients with palinopsia. Routine labs such as a complete metabolic panel and complete blood count (CBC) may be done to check for metabolic disturbances or hint at the presence of a neoplasm (Gersztenkorn and Lee 2014). Other diagnostic tests can be performed as needed. These would include structural or functional neuroimaging, electroencephalogram (EEG), electroretinogram (ERG), visual evoked potential (VEP), lumbar puncture, or drug screen (Gersztenkorn and Lee 2014).

Differential Diagnosis

(a) Physiological afterimages
(b) Visual hallucinations
(c) Illusions
(d) Polyopia
(e) Diplopia

Prophylaxis

Therapy

The treatment of palinopsia greatly differs according to the etiology, but many forms of treatment have shown anecdotal but variable positive results.

Prognosis

The prognosis for palinopsia differs according to the etiology.

Epidemiology

Palinopsia can affect patients of any age, either gender, and all races.

Cross-References

▶ Drugs: Hallucinations

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Palpebral Conjunctiva

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Synonyms

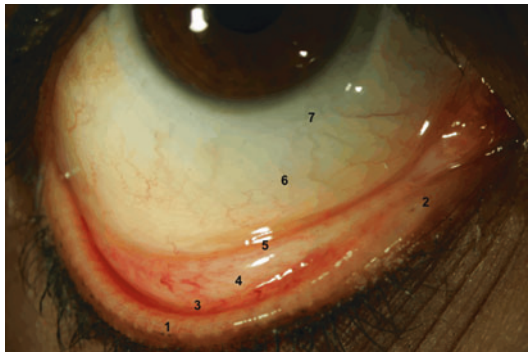
Conjunctiva; Tarsal conjunctiva

Definition

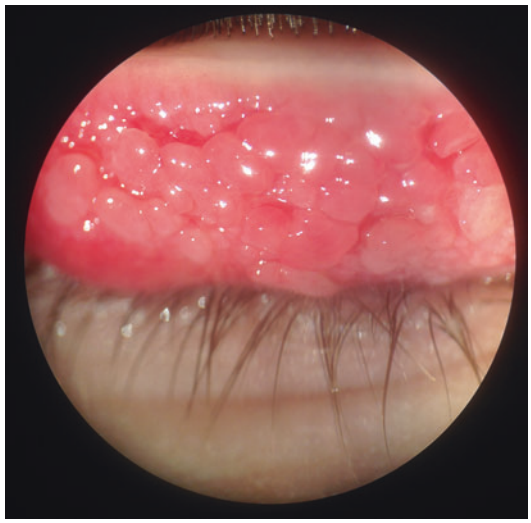
The conjunctiva is a mucous membrane that can be divided into three anatomical subdivisions: (1) palpebral, (2) forniceal, and (3) bulbar. The palpebral conjunctiva is firmly attached to both the upper and lower tarsi; however it is more firmly attached to the upper tarsus.

Structure

The palpebral conjunctiva begins at the posterior third of the meibomian gland openings of each eyelid. At this mucocutaneous junction, the cells change from a keratinized stratified squamous



Palpebral Conjunctiva, Fig. 1 Colored slit-lamp photograph of right lower eyelid. (*1*) Mucocutaneous junction, (*2*) lacrimal punctum, (*3*) subtarsal groove, (*4*) tarsal conjunctiva, (*5*) forniceal conjunctiva, (*6*) bulbar conjunctiva, and (*7*) contact lens on limbus



Palpebral Conjunctiva, Fig. 2 Clinical photograph of giant papillary conjunctivitis (attached)

epithelium of the skin to a nonkeratinized stratified squamous epithelium of the marginal conjunctiva. Nasally, this mucocutaneous junction is where the conjunctiva connects to the lacrimal puncta (Figs. 1 and 2).

Two millimeters from the eyelid margin on the palpebral conjunctiva is a shallow grove known as the subtarsal groove. This groove lies parallel to the eyelid margin and marks the transition from a stratified squamous epithelium of the marginal conjunctiva to a cuboidal epithelium of the palpebral conjunctiva. This groove acts as a trap for foreign bodies, bacteria, and cellular debris before they reach the cornea and bulbar conjunctiva. There are a series of small saccular mucus glands between the eyelid margin and tarsal groove that open to the conjunctival surface.

All three geographic areas of the conjunctiva consist of nonkeratinized epithelium over the substantia propria. The nasal palpebral conjunctiva contains numerous crypts known as Henle's mucus crypts. In the central palpebral conjunctiva, these crypts form a network of subepithelial grooves. The grooves become tunnels with interconnections that open onto the ocular surface. These grooves and tunnels divide the conjunctiva into papillae. Mucin-secreting goblet cells, mucous glands, and clusters of cells known as the glands of Manz are also scattered within the epithelium. The fornices contain more goblet cells than the tarsal and bulbar conjunctivas; the inferior and nasal conjunctivas have more goblet cells than the superior and temporal conjunctiva.

The palpebral conjunctiva has a rich sensory innervation from the ophthalmic division of the trigeminal nerve (V1). These nerves are nociceptors that are sensitive to energy, heat, chemical irritants, and chemical mediators. There are no motor fibers in the conjunctiva. The conjunctiva receives blood from the muscular, medial palpebral, and lacrimal branches of the ophthalmic artery.

Function

The palpebral conjunctiva plays a key role in:

- Ocular surface integrity
- Ocular surface lubrication
- Protection of the globe
- Absorption of topical medications

Clinical Relevance

The conjunctiva is best examined using slit-lamp biomicroscopy by lowering the lower eyelid and everting the upper eyelid.

Local and systemic diseases may manifest themselves in the palpebral conjunctiva. The palpebral conjunctiva is examined for follicles and papillae. Follicles represent hypertrophy of the underlying lymphoid tissue and do not have prominent central vessels. Papillae are tiny, dome-shaped nodules with a central core of hyperemic blood vessels surrounded by edema and inflammatory cells; papillary conjunctivitis may show a cobblestone arrangement of these flattened nodules.

Follicular reactions are most commonly due to viral, chlamydial, allergic, and toxic etiologies. Topical medications such as brimonidine or over-the-counter ophthalmic decongestants have been reported to cause follicular conjunctivitis. Papillary reactions are most commonly associated with allergic immune responses (e.g., vernal and atopic keratoconjunctivitis) or foreign bodies (e.g., contact lens wear).

In addition to follicular and papillary reactions, other common pathologies found in the palpebral conjunctiva are granulomas, membranes, pseudomembranes, scarring, and foreign bodies. Though rare, nevi, dysplasias, and carcinomas involving the palpebral conjunctiva have been reported.

Cross-References

- ▶ Conjunctiva
- ▶ Conjunctival Tumors
- ▶ Hyperemia, Conjunctival
- ▶ Melanomas, Conjunctival
- ▶ Pigmented Lesions of the Conjunctiva
- ▶ Tarsal Conjunctiva

Further Reading

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Palpebral Vernal Conjunctivitis/ Keratoconjunctivitis

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Synonyms

Vernal conjunctivitis

Definition

Vernal keratoconjunctivitis (VKC) is a chronic, bilateral form of ocular surface allergic inflammation. There are two forms of VKC: palpebral and limbal. The palpebral type predominantly involves the upper tarsal conjunctiva, while the limbal form affects the cornea, limbus, and sclera. The two types are not exclusive and patients may present with signs of both.

Etiology

Vernal keratoconjunctivitis is an immune-mediated hypersensitivity reaction. The primary pathway likely involves a type I immediate hypersensitivity response. Lymphoid follicles in the conjunctiva are stimulated to produce IgE, which leads to mast cell degranulation and release of histamine in addition to other compounds. This results in vasodilation and recruitment of inflammatory cells such as eosinophils. Type IV delayed hypersensitivity may also play a role, resulting in

a common pathway of IgE production, mast cell degranulation, and inflammatory cell recruitment (De Smedt et al. 2013).

Clinical Presentation

Patients with VKC typically have bilateral complaints of photophobia, intense itching, tearing, and a thick mucus discharge. They may also experience burning, foreign body sensation, pain, and blurred vision (De Smedt et al. 2013).

The hallmark of palpebral VKC is the presence of discrete, giant cobblestone-like papillae on the upper palpebral conjunctiva. Examination may also reveal conjunctival hyperemia, a sticky nonpurulent mucus discharge, blepharospasm, and ptosis.

Diagnosis

The diagnosis of palpebral VKC is made clinically, with typical signs on external examination in the classic patient population. Diagnosis may be aided by conjunctival scrapings showing eosinophilic predominance and tear analysis showing increased IgE levels, but these laboratory tests have low sensitivity and specificity. Conjunctival biopsies can show increased mast cells, eosinophils, and lymphocytes (Bonini et al. 2004). Histologically, giant papillae are characterized by a squamous epithelial hyperplasia with an extensive inflammatory infiltrate into the fibrous tissue (De Smedt et al. 2013).

Differential Diagnosis

Atopic keratoconjunctivitis (perennial, lower tarsus).

Giant papillary conjunctivitis (related to contact lens use).

Therapy

First-line therapy for VKC is with dual-acting topical antihistamines and mast cell stabilizers. These inhibit mast cell degranulation as well as block histamine receptors in the conjunctiva and eyelids. Topical corticosteroids can be considered if there is poor response. Topical calcineurin inhibitors such as cyclosporine have also been shown to be effective (Kumar 2009).

Nonspecific therapy includes avoidance of triggers, avoidance of eye rubbing to decrease mast cell degranulation, artificial tears, and cool compresses.

Prognosis

The prognosis of palpebral VKC is generally excellent, as it is most often a self-limiting disease with spontaneous resolution after puberty.

Epidemiology

Vernal keratoconjunctivitis is typically seen in young male patients in their first decade of life who live in warm, dry, subtropical climates. Exacerbations of this disease usually occur in the spring, but in a minority of patients may also occur in the winter and can develop into a chronic, perennial disease (De Smedt et al. 2013). There is an association of this disease with other atopic diseases such as asthma and allergic rhinitis, as well as with a family history of atopy (Kumar 2009).

Cross-References

- ▶ Allergic Conjunctivitis
- ▶ Giant Papillary (Contact Lens-Induced) Conjunctivitis Disease

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Pannus/Micropannus

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Synonyms

Corneal neovascularization; Corneal vascularization; Fibrovascular pannus

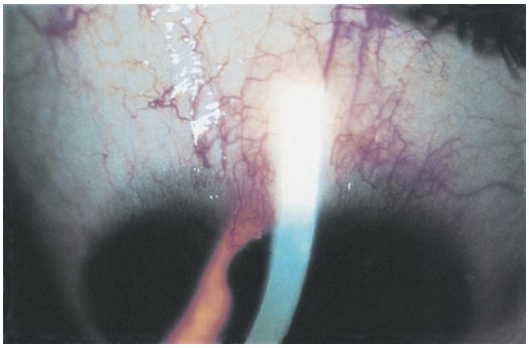
Definition

Pathologic ingrowth of vessels from the limbal vascular plexus into the cornea (pannus is a Latin word meaning carpet).

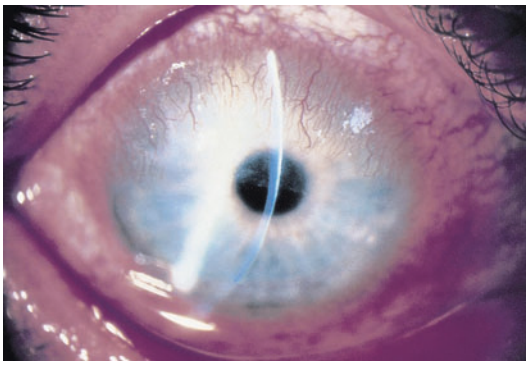
In general, the mainspring of this pathology is ocular surface inflammation. When blood vessels and fibrous connective tissue from the limbus grow onto the peripheral cornea, secondary to inflammation, the result is a *fibrovascular pannus*. A vascular pannus could be seen in any corneal location depending upon the inciting inflammation. In adults, pannus usually extends from the peripheral cornea toward the central cornea and is generally flat. In infants and small children, pannus may develop as a hyperplastic reaction to the inflammation, and it could be seen as an elevated lesion.

There are three basic cells involving in formation of subepithelial vascular fibrosis: leukocytes, proliferating vascular endothelial cells, and active fibroblasts that secrete an extracellular connective tissue matrix. Also, there are three basic ways for generation of this pathology:

1. Following mild insults (e.g., contact lens-induced hypoxia), in which a very fine sheet of fibrovascular tissue slowly migrates from the limbus
2. After severe insults (e.g., alkali burns) in which a thick layer of exuberant fibrovascular tissue may develop across the entire cornea
3. In the base of chronic long-standing insult such as trachomatous eyelid scarring and entropion where a progressive dense pannus spreads centrally from the limbus (Krachmer et al. 2011).



Pannus/Micropannus, Fig. 1 Superior corneal micropannus. American Academy of Ophthalmology, ONE Network Image Collection

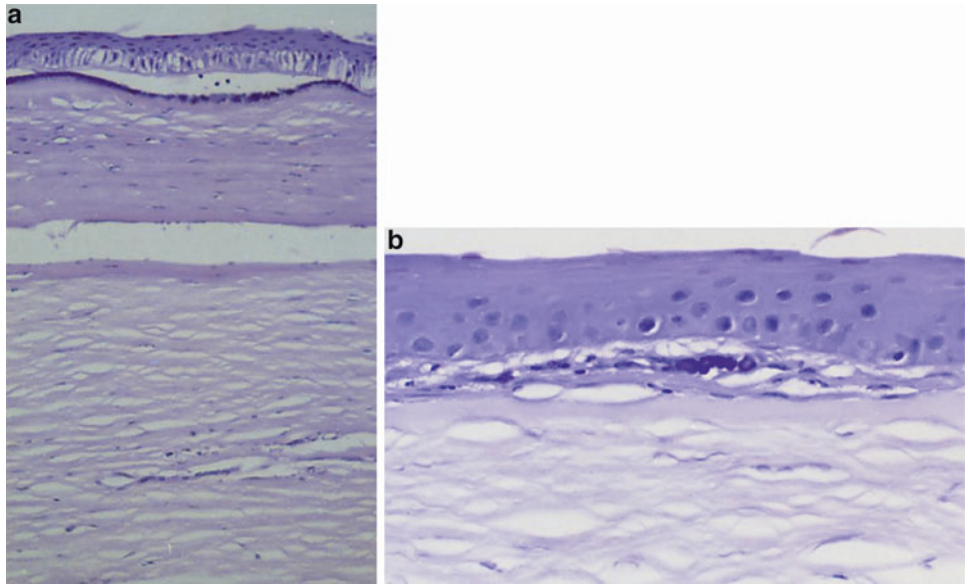


Pannus/Micropannus, Fig. 2 Corneal pannus, subepithelial fibrous ingrowth. American Academy of Ophthalmology, ONE Network Image Collection

In general, fibrous or vascular tissue spread between the epithelial basement membrane and Bowman's layer, but neither of them become fibrotic or vascularized. Sometimes, a fibrovascular tissue replaces the Bowman's layer or grows into the anterior stroma immediately posterior to Bowman's layer (Figs. 1, 2, and 3).

Etiology

There are so many situations that could eventuate to pannus formation: infection such as inclusion conjunctivitis, trachoma, herpes simplex



Pannus/Micropannus, Fig. 3 Pannus, degenerative, and fibrovascular. American Academy of Ophthalmology, ONE Network Image Collection

infection, contact lens wear, trauma, chemical burn, immunologic diseases such as ocular rosacea, staphylococcal hypersensitivity, vernal keratoconjunctivitis, superior limbic keratoconjunctivitis, degeneration or intraocular events such as uveitis, glaucoma, and phthisis bulbi.

Several theories have been proposed for the development of contact lens-induced pannus. Mechanical rubbing from poorly fitting contact lenses could damage the limbal stem cells. This may cause perilimbal capillaries to grow between the corneal epithelium and Bowman's layer, forming a pannus.

These capillaries are usually accompanied by fibroblasts which produce collagen and induce Bowman's layer destruction, producing a superficial corneal scar and irregular astigmatism.

Mechanical pressure from blinking over contact lens may contribute to superior pannus formation. Long-term hypoxia from low oxygen-permeable soft contact lenses or chronic use of tight-fitted lenses could also result in pannus.

In the background of limbal stem cell deficiency, fibrovascular pannus formation is categorized as a type III corneal healing pattern which corresponds to a grade III injury. In this grade of injury, there has been complete loss of limbal stem cells but preservation of source of proximal conjunctival epithelium (Copeland and Afshari 2013).

In this pattern, delayed reepithelialization with conjunctival epithelium may occur in the next few weeks or months, although it will be with fibrovascular pannus (conjunctivalization) of the ocular surface, and the ultimate outcome is a vascularized cornea (Krachmer et al. 2011).

Clinical Presentation

Symptoms: may be asymptomatic or may result in mild to severe visual loss, ocular redness, stinging, and foreign body sensation

Signs:

Two patterns of pannus may be seen:

- Fine, superficial neovascularization of the cornea that is most commonly seen in contact lens wearers and also can be associated with blepharitis, superior limbic keratoconjunctivitis, vernal conjunctivitis, and many others

- Deep stromal neovascularization that could be seen in patients with extended wear contact lens, chronic blepharoconjunctivitis, keratitis, trachoma, toxic chemical injuries, graft rejection, and phlyctenulosis (Krachmer et al. 2011).

Diagnostics (Lab Diagnostics)

Diagnosis of pannus is usually made on the basis of characteristic clinical signs. Confocal microscopy and optical coherence tomography (OCT) could be used in difficult cases. Pathologic study could be confirmatory after fibrovascular sheet excision over the cornea.

Differential Diagnosis

Corneal neovascularization could occur in so many situations: infections (such as inclusion conjunctivitis, trachoma, and herpes simplex infection), contact lens wear, trauma, chemical burn, immunologic diseases (such as ocular rosacea, staphylococcal hypersensitivity, and vernal keratoconjunctivitis), superior limbic keratoconjunctivitis, degeneration or intraocular events such as uveitis, glaucoma, and phthisis bulbi.

Subepithelial opacities can be seen in epidemic keratoconjunctivitis, chlamydia, herpes simplex, staphylococcal disease, and nummular keratitis (Krachmer et al. 2011).

Prophylaxis

The main resource for prophylaxis is subsiding background inflammation and treating triggering condition.

Therapy

- Supportive, which directed at eliminating the underlying condition.
- Topical corticosteroid may be applied for subsiding background inflammation.
- Diathermy and thermal cautery of large feeding vessels could be used for ligating intrastromal vessels.
- Corneal laser photocoagulation has been among the surgical modalities to treat pannus.
- Intrastromal injection of anti-vascular endothelial growth factor (VEGF) agents could be used for regressing corneal neovascularization.
- Limbal stem cell grafting may be required in eyes with severe limbal stem cell deficiency such as chemical injuries and Steven-Johnson syndrome (Krachmer et al. 2011).

Prognosis

The prognosis could be differed from mild cases of micropannus formation with minimal change in corneal surface and good visual acuity to severe cases of extensive fibrovascular pannus with corneal surface destruction and severe visual loss.

Epidemiology

Unknown, it is dependent to underlying disorder.

Cross-References

► Corneal Neovascularization

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Papilla Nervi Optici

► Fundamental Considerations Regarding the Optic Nerve

Papillae: Overview

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Synonyms

Raised conjunctival lesions

Definition

Papillae are raised inflammatory lesions that present typically in the palpebral conjunctiva and in the limbal bulbar conjunctiva attached to the deeper fibrous layer (Kanski and Bowling 2011). Papillae contain a vascular core, differentiating them from follicles. Follicles are lymphatic structures.

Structure

Papillae can appear in several forms and sizes. Micropapillae present as an eclectic, mosaic pattern of raised red dots, or a "goose-pimple" appearance (Yanoff and Duker 2014). This presentation is seen to be due to a central vascular channel (Kanski and Bowling 2011). Macropapillae (<1 mm) and giant papillae (>1 mm) occur in tandem with inflammation. These larger papillae may have a cobblestone appearance.

Histology of the papillae reveals hyperplastic conjunctival epithelium with a fibrovascular core and subepithelial stromal infiltration with inflammatory cells (Kanski and Bowling 2011). Prolongation of inflammatory changes can result in crypt formation with goblet cells, superficial stromal hyalinization, and scarring.

Function

Papillae occur due to conjunctival inflammation that is limited by the fibrous septa, resulting in the appearance of raised, vascular red dots (Kanski and Bowling 2011).

Clinical Relevance

Several ophthalmological diseases may present with papillae. These include but are not limited to bacterial conjunctivitis, allergic conjunctivitis, giant papillary conjunctivitis, vernal conjunctivitis, chronic marginal blepharitis, and contact lens wear (Kanski 2009).

Cross-References

- ▶ Allergic Conjunctivitis
- ▶ Conjunctivitis
- ▶ Vernal Conjunctivitis

References

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Papilloma

- ▶ Papillomas, Eyelid
- ▶ Squamous Cell Papillomas of Eyelid

Papillomas, Conjunctival

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Synonyms

Conjunctival squamous cell papilloma

Definition

Conjunctival papillomas are benign squamous epithelial growths of viral origin (human papillomavirus) with limited tendency toward malignancy (Bailey and Guethlein 1990). They may develop from the bulbar or palpebral conjunctiva. They are categorized as infectious, squamous, limbal, or inverted based upon clinical and patient history. They may also be classified according to gross appearance as either pedunculated or sessile.

Etiology

Infectious squamous conjunctival papillomas have a strong association with human papillomavirus (HPV) types 6 and 11 (Minchiotti et al. 2006). HPV is transmitted via direct human contact and typically produces benign tumor growths with minimal risk for malignancy. HPV 33 is also associated with conjunctival papillomas. The recurrence rate for conjunctival papillomas of viral etiology is quite high; limbal papillomas have a 40% recurrence rate.

Noninfectious causes of conjunctival papillomas may include UV radiation exposure (Bailey and Guethlein 1990).

Clinical Presentation

Clinical History

Squamous cell papillomas are associated with younger populations (<20 years), HPV infection, prior tumor excision, history of extraocular warts, similar history in a sibling, and no decrease in visual acuity (Bailey and Guethlein 1990).

Limbal papillomas are found in older adults, history of UV radiation, possible decrease in visual acuity, history of refractive chronic conjunctivitis, and recurrence after excision.

Physical Exam

Tumor location: Most conjunctival papillomas are isolated lesions. About 25% of lesions involving the caruncle are papillomas. Squamous cell carcinoma is commonly found only at the interpalpebral zone and rarely found far from the limbus.

Tumor color: Pigmented lesion hints at melanocytic origin. Yellow lesions may indicate a xanthoma. Salmon-coloration suggests lymphoid tumors.

Tumor growth pattern: Papillomas have solitary growth patterns as opposed to more diffusely growing lesions like sebaceous carcinomas with pagetoid growth.

Tumor texture: Conjunctival epithelial tumors tend to have raised, cobblestone appearance. Tumors with smoother epithelial surface tend to arise from the substantia propria. Moreover, abrupt borders exist between normal conjunctiva and tumor.

Squamous cell and limbal papillomas can be differentiated further by physical exam. Squamous papillomas tend to occur bilaterally and numerous at the inferior fornix commonly. Limbal are unilateral and solitary and occur at the limbus or bulbar conjunctiva.

Diagnostics (Lab Diagnostics)

Definitive diagnosis is typically obtained via biopsy (Eagle 1999). Biopsy is conducted to rule out malignancy and to determine surgical margins in poorly defined lesions. Frozen sections may also be acquired to rule out surgical margins for tumor.

Histology will help to determine the type of lesion. Squamous cell papillomas tend to have multiple branching fronds spreading outward from a narrow pedunculated base. Inflammation may be associated with these fronds, and the basement membrane is intact. In contrast, limbal papillomas tend to be sessile lesions that emerge from a broad base. The basement membrane is intact. Less commonly found, inverted papillomas exhibit exophytic and endophytic growth patterns.

Differential Diagnosis

Ichthyosis
Sebaceous Gland Carcinoma
Squamous Cell Carcinoma of the Conjunctiva

Prophylaxis

HPV vaccine and avoidance

Therapy

Surgery is indicated for conjunctival papillomas (Bailey and Guethlein 1990). Excisional biopsy is preferred to incisional biopsy when possible for patients. Seeding is a risk following excision. Observation and coordination with patient's wishes is important for deciding on therapy.

Squamous cell papillomas may regress over time. However, cryotherapy is indicated for squamous cell papillomas to reduce scarring and recurrence rate (Omohundro and Elliott 1970). This procedure is contraindicated for limbal papillomas because it does not help rule out malignant changes.

In cases where surgical excision, cryoablation, and other modalities have failed, suggested adjunctive therapies include interferon alpha (Schechter et al. 2002).

Prognosis

Positive prognosis for patients (Bailey and Guethlein 1990). However, recurrence is not uncommon for viral papillomas. Patients should receive follow-up to track recurrences.

Epidemiology

Limited prevalence data exists for conjunctival papillomas. However, it is well established that there is a strong association between HPV and squamous cell conjunctival papillomas (Minchiotti et al. 2006).

Squamous cell papillomas are found in typically children and young adults less than 20 years of age. Limbal cell papillomas typically occur in older adults.

Conjunctival papillomas are not life threatening and rather may cause cosmetic and visual discomfort for patients.

Cross-References

- ▶ Human Papillomavirus
- ▶ Sebaceous Gland Carcinoma
- ▶ Squamous Cell Carcinoma, of the Conjunctiva

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Papillomas, Eyelid

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Synonyms

Cutaneous horn; Follicular keratosis; Papilloma; Pseudoepitheliomatous hyperplasia; Seborrheic keratosis; Squamous papilloma; Verruca vulgaris

Definition

Papilloma is a nonspecific term that describes benign epithelial proliferations of the eyelid.

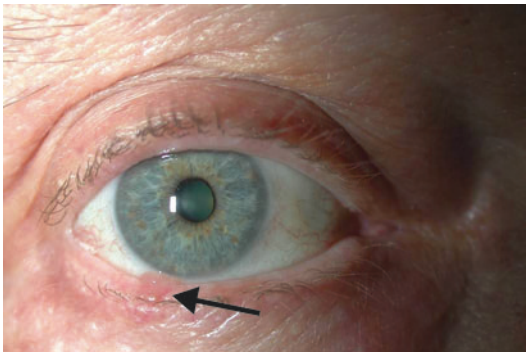
Characteristics

Squamous papilloma is the most common benign growth of the eyelid. It may present as sessile or pedunculated, solitary or multiple lesions. Lesions tend to be slow growing. Verruca vulgaris is a specific squamous papilloma associated with the human papilloma virus (type VI and XI). The differential diagnosis for papillomas includes nevi, fibroma, epithelioma, actinic keratosis, verruca vulgaris, and seborrheic keratosis. Treatment involves observation, surgical excision, or carbon dioxide laser ablation.

Seborrheic keratosis is a common lesion of the eyelid that has a characteristic smooth, greasy, stuck-on appearance, with variable pigmentation. It may resemble squamous cell carcinoma. Treatment involves superficial shave excision at the junction between the dermis and epidermis. Inverted follicular keratosis is a term associated with irritated seborrheic lesions.

Pseudoepitheliomatous hyperplasia or pseudocarcinomatous hyperplasia refers to reactive changes in the epidermis adjacent to areas of previously treated cryosurgery or surgical wounds. It may be mistaken as a malignant lesion.

Cutaneous horn describes changes related to hyperkeratosis. These changes may be associated with a variety of benign or malignant epithelial lesions (Fig. 1) (Shields and Shields 1999; Albert and Jakobiec 2008).



Papillomas, Eyelid, Fig. 1 Lower eyelid margin papilloma (arrow)

Differential Diagnosis

Seborrheic keratosis
Pseudoepitheliomatous hyperplasia
Verruca vulgaris
Cutaneous horn

Management

See individual entities for further information.

Cross-References

- ▶ Cutaneous Horn
- ▶ Pseudoepitheliomatous Hyperplasia
- ▶ Seborrheic Keratosis
- ▶ Verruca Vulgaris

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P

Papillomaviridae

▶ Human Papilloma Viruses, Ocular Infection

Parabulbar Anesthesia

▶ Peribulbar Anesthesia

Paramedian Pontine Reticular Formation and Abducens Nucleus

▶ Horizontal Gaze Center

Paranasal Sinuses

► Sinuses

Paraneoplastic Retinopathy

► Cancer-Associated Retinopathy

Parasellar Lesions

► Chiasmal Disorders

Parasites

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Synonyms

Parasitic diseases; Parasitic infections

Definition

Parasitic disease of the eye includes any infection, infestation, or inflammation (e.g., neuro- and chorioretinitis, uveitis, keratitis) caused by any number of organisms (ranging from protozoans to helminths).

Structure

The manifestations of parasitic infections can either stem from systemic infection or be ocularly localized. Infections are wide ranging in their presentation. Detailed below are some of the most common etiologic agents and their ocular manifestations.

Clinical Relevance

(A) Parasitic retinitis and its causative organisms.

Toxoplasmosis (causative agent: *Toxoplasma gondii*) produces a necrotizing retinitis and is the most common cause of infectious retinitis in immunocompetent patients. Common signs include decreased vision, photophobia, floaters, vascular sheathing, full-thickness retinal necrosis, and a fluffy, yellow-white retinal lesion with overlying vitreous reaction. Toxoplasmosis infection is categorized as either **acquired** (from eating undercooked meat) or **congenital** (from transplacental transmission). *T. gondii* is an obligate intracellular protozoan, and its most definitive host is domesticated felines, though it can also infest other mammals (principally livestock) as well as humans. Infection is initiated by ingestion of the oocysts from feces of the definitive host in contaminated food or water or from the ingestion of tissue cysts (which include bradyzoites), that are the product of infection in the animal itself. Tissue disruption is caused by the active form of the protozoan, called tachyzoites.

Complications of toxoplasma infection include direct involvement of the macula or secondary optic nerve head involvement due to a juxtapapillary lesion. Less common complications include primary optic nerve head involvement, which can present as anterior ischemic optic neuropathy or if the inflammatory focus of the primary infection can induce occlusion of a larger blood vessel, triggering ischemia. Cases of choroidal neovascularization, serous retinal detachment, tractional retinal detachment, and macular edema have all been reported in conjunction with toxoplasma.

Treatment is geared toward reducing the acute inflammation and the risk of permanent visual loss by reducing scarring. Small lesions do not usually require treatment if they are peripherally located, though severe or posterior infections are treated for up to 6 weeks with pyrimethamine and

trisulfapyrimidine, and patients are usually given leucovorin calcium to prevent bone marrow suppression. Clindamycin is an alternative therapy. Complications (including increased intraocular pressure) are managed as they would be otherwise.

Taenia solium is a common tapeworm that infects swine and humans. Like many cestodes, its life cycle begins in humans with the ingestion of eggs or gravid proglottids. Larvae migrate into the host tissue to cause cysticercosis. It can occasionally cause conjunctivitis but usually invades the retina, choroid, or vitreous. Diagnosis is made from a positive complement fixation or precipitin test or by demonstrating the presence of the organism in the gastrointestinal tract. Eosinophilia is usually present as well.

Treatment for *T. solium* requires excision of the ocular lesion and niclosamide (or praziquantel) for the tapeworm infection. Parasitic conjunctivitis and its causative organisms (Garcia et al. 2013).

Pthirus pubis infection is caused by pubic lice and may infest the cilia and the margins of the eyelids. A toxic follicular conjunctivitis in children and a papillary conjunctivitis in adults is caused by the release of an chemical irritant. Intense itching is usually present. Diagnosis is confirmed by finding either the adult organism or oval-shaped nits.

Treatment for *P. pubis* includes lindane or pyrethrins, applied to both the pubic area and the lash margins after removal of the nits. All clothes and accessories that may have come in contact should be washed carefully.

Ophthalmomyiasis is an infection caused by the larvae of flies (common species include *Musca domestica*, *Fannia*, and *Oestrus ovis*), which can invade either necrotic or healthy tissue. External wounds and ingestion are the most common routes of transmission. The infection usually occurs on the surface of the eye, though cases have been reported with infection in intraocular tissues.

Treatment is the removal of the larvae after the application of a topical anesthetic (Kean et al. 1991).

Thelazia californiensis is a roundworm that usually inhabits the eyes of domesticated dogs, but also infects a range of mammals (feral and domestic). Accidental infection through contact has been reported. Treatment is the removal of the larvae after the application of a topical anesthetic.

Loa loa is a common eye worm in sub-Saharan Africa and resides in the connective tissue of primates. A vector fly (such as the horse or mango fly) ingests microfilariae from an infected human host, which then move to the fat body of the insect and develop into larvae. The infective form of the larvae travels to the proboscis and is then transmitted to an uninfected host upon a bite. The infective form matures into microfilariae which disseminate in various host tissues. Diagnosis is made by identifying the organism in a blood smear, usually corroborated by mild eosinophilia (Cook et al. 2009). Treatment is diethylcarbamazine.

Ascaris lumbricoides is a roundworm that can cause a very painful and toxic conjunctivitis from the exposure to infected tissue of other animals and must be treated by rapid and thorough irrigation of the conjunctiva (Gunn and Pitt 2012).

Trichinella spiralis is a nematode parasite and more commonly the cause of trichinosis, which can be asymptomatic or cause general enteric symptoms. It completes its life cycle in a single host, beginning with the ingestion of cysts in infected meat. The larvae in these cysts are released in the stomach and migrate to the intestines, where they reproduce as anaerobic or facultative anaerobes. The larvae then gain access to the circulation and migrate throughout the host tissues and can cause myocarditis or encephalitis as well as infection of the muscle and cutaneous tissue. Most patients have a chemosis (a pale swelling over the lateral and medial rectus muscles) which may last a week or more (Gunn and Pitt 2012).

Schistosoma haematobium is more commonly the cause of schistosomiasis (bilharziasis), which is endemic in the regions bordering the Nile River. It is a

trematode (flatworm) that uses snails as its intermediate host. Infective free-swimming larval cercariae burrow into the human skin and enter the bloodstream and migrate to the liver. They then migrate to the urinary bladder to reproduce and be further disseminated. *S. haematobium* infection results in a characteristic granuloma that has lymphocytes, plasma cells, giant cells, and eosinophils surrounding the ova's various different stages. Conjunctival lesions are similar to *Trichinella* (Cook et al. 2009).

Treatment of choice includes praziquantel or antimonials and excision of the granuloma.

Cross-References

- ▶ Antibiotics for Eye Infections
- ▶ Trichinella spiralis Trichinosis, Orbital Infection Caused by

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Parasitic Diseases

- ▶ Parasites

Parasitic Infections

- ▶ Parasites

Parietal Radiations Lesion

- ▶ Retrochiasmal Disorders

Parinaud (Dorsal Midbrain) Syndrome

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Synonyms

Dorsal midbrain syndrome; Parinaud's syndrome; Vertical gaze palsy

Definition

Parinaud syndrome (PS) is a collection of eye movement and pupillary response dysfunction most commonly caused by compression or lesion of the dorsal midbrain. Named after the French ophthalmologist Henri Parinaud (1844–1905), it is most commonly associated with vertical gaze palsy.

Etiology

PS can be caused by any lesion (e.g., compression, ischemia, inflammatory) of the dorsal midbrain. In young patients, the most common cause is a tumor of the pineal region (e.g., dysgerminoma or pinealoma). In younger to middle-aged women, multiple sclerosis and, in older patients, stroke are common causes of PS. However, any damage to the riMLF, mesencephalic tectum, including the superior colliculus, oculomotor nuclei, and Edinger-Westphal nuclei can present with PS including trauma, obstructive hydrocephalus (ventriculoperitoneal shunt failure), hemorrhage, cerebral arteriovenous malformation, toxoplasmosis, neoplasms of the posterior cranial fossa, and aneurysms.

Clinical Presentation

The defining characteristics of PS are upgaze paralysis (downward gaze is often preserved), light-near dissociation of the pupils, accommodative paresis, convergence-retraction nystagmus, and eyelid retraction (Collier's sign). Later conjugate downgaze palsy or downgaze preference (setting-sun sign) may occur. Less common clinical findings in PS include: papilledema, spasm of accommodation, thalamic esotropia, seesaw nystagmus, skew deviation, oculomotor nerve palsy, trochlear nerve palsy, and internuclear ophthalmoplegia.

Diagnostics

Neuroimaging is essential to accurately diagnose and effectively treat patients with PS.

Differential Diagnosis

Any lesion in the dorsal midbrain can produce PS including neoplasm (e.g., pinealoma, pineal cysts, tumors of the midbrain), multiple sclerosis, stroke, aneurysm, obstructive hydrocephalus (commonly ventriculoperitoneal shunt failure), hemorrhage, cerebral arteriovenous malformation, and infection (e.g., toxoplasmosis, syphilis).

Prophylaxis

No method of prophylaxis has been established.

Therapy

Therapy for PS should be directed to the underlying etiology.

Prognosis

The prognosis depends on the underlying etiology.

Epidemiology

PS in children is commonly caused by pinealomas or hydrocephalus. In middle-aged women, multiple sclerosis is often the cause. In older patients, stroke and hydrocephalus are the most common etiological agents.

Cross-References

- ▶ Collier's Sign
- ▶ Dorsal Midbrain (Parinaud) Syndrome, Convergence-Retraction Nystagmus, Eyelid Retraction
- ▶ Light-Near Dissociation
- ▶ Ophthalmoplegia, Internuclear
- ▶ Setting Sun Sign
- ▶ Skew Deviation
- ▶ Vertical Gaze Palsy

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Parinaud's Syndrome

▶ Dorsal Midbrain (Parinaud) Syndrome, Convergence-Retraction Nystagmus, Eyelid Retraction
▶ Parinaud (Dorsal Midbrain) Syndrome

Pars Plana Vitrectomy

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Definition

Surgical procedure to remove the vitreous or part thereof by accessing vitreous cave via pars plana.

Epidemiology

Formerly related to a large variety of serious complications, vitrectomy – especially small-gauge pars plana vitrectomy – has become a widely used technique for a large number of pathologies. To date approximately 200,000 vitrectomies are performed in the USA per year.

History

Robert Machemer first established pars plana vitrectomy as a single-port 19-gauge procedure in 1969. Using this technique, it was possible to remove part of the vitreous in case of vitreous opacities (Fabian and Moisseiev 2011). Further technical improvement established pars plana vitrectomy as a widely used technique for a large variety of pathologies. Nowadays pars plana vitrectomy is used for surgery of retinal detachment, of vitreous pathologies, and of vitreoretinal interface pathologies (such as macular pucker or macular hole formation).

Clinical Features

In pars plana vitrectomy, accession of the vitreous cave is via pars plana. In this anatomical region posterior of the ciliary body, perforation of the eye is possible, as no retinal tear has to be feared. Thus, sclerostomy (either using an incisional knife or a trocar) is performed 3.5–4 mm from the limbus. In a usual setting, pars plana vitrectomy is performed as a three-port vitrectomy: While the temporal lower quadrant is site for the infusion providing constant pressure, two additional sclerostomies are within the upper quadrants providing bimanual accession for the surgeon.

Excision of the vitreous is usually performed using a specially designed cutter. This cutting tool usually consists of a tube with an oscillating knife. By applying suction, the vitreous is sucked into the tube and cut by the oscillating knife.

Critical steps during vitrectomy include induction of posterior vitreous detachment and excision of the anterior part of the vitreous (vitreous base).

While for a long time, pars plana vitrectomy has been performed using 20-gauge instruments, the majority of vitrectomies nowadays are performed using a trocar system and smaller instruments (23 gauge, 25 gauge, or 27 gauge) Recchia et al. (2010).

There are a large variety of instruments for surgery such as forceps, lights, and different cutters.

Tests

Efficacy of this surgical procedure for a large number of pathologies has been demonstrated.

Etiology

See "History."

Treatment

There are several indications for pars plana vitrectomy: vitreous hemorrhage, retinal detachment, macular pucker, or complications during cataract extraction to name a few.

Cross-References

- ▶ Macular Holes
- ▶ Pars Plana; Pars Plicata
- ▶ Retinal Detachment
- ▶ Vitrectomy

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Pars Plana; Pars Plicata

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Synonyms

Ciliary body

Definition

The ciliary body is divided into an anterior ring, the pars plicata, and a posterior ring, the pars plana. The pars plicata is 1.5 mm wide and contains 70–75 fingerlike projections called ciliary processes. The pars plana is 3.5–4.0 mm wide in an adult eye and is an ideal location for instrument insertion or intravitreal injection due to minimal potential damage to the eye. Both the pars plicata and pars plana are covered by a bilayered ciliary epithelium. The inner nonpigmented epithelium is the main source of aqueous humor in the eye. The outer pigmented epithelium creates the blood-aqueous barrier.

Cross-References

- ▶ Accommodation, Cataract
- ▶ Aqueous Humor
- ▶ Ciliary Body
- ▶ Vitrectomy

Partial Coherence Interferometry

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Synonyms

Optical biometry

Definition

Partial coherence interferometry is an optical biometry of intraocular distances in the eye.

Purpose

Partial coherence interferometry allows precise measurement of central corneal thickness, anterior chamber depth, lens thickness, and axial length of the eye.

Principle

In dual-beam partial coherence interferometry, a Michelson interferometer splits an infrared light beam of high spatial coherence but very short coherence length into two parts, forming a coaxial dual beam. This dual light beam, containing two

beam components with a mutual time delay of twice the interferometer arm length difference introduced by the interferometer, illuminates the eye. Both components are reflected at several intraocular interfaces that separate media of different refractive indices. If the delay of these two light beam components produced by the interferometer equals an intraocular distance within the coherence length of the light source, an interference signal (called partial coherence interferometry signal) is detected, similar to that of ultrasound A-scan. In anterior segment partial coherence interferometry, longer wavelengths are applied as compared to measurement of the axial length.

Indication

Optical biometry of the eye prior to cataract or refractive surgery.

Contraindication

Patients with dense cataracts or patients unable to cooperate or fixate during the measurement process.

Advantage/Disadvantage

Partial coherence interferometry is a highly precise and reliable method for biometry of the eye. The precision of measurement seems to be higher than in ultrasound biometry. In contrast to ultrasound contact biometry, the measurement is independent of the examiner's ability to locate the correct position of the eye during measurement. In contrast to ultrasonic biometry, noncontact anterior segment partial coherence interferometry reduces the risk of injuring the cornea during measurement. However, partial coherence interferometry cannot be applied in patients with opaque media.

Cross-References

▶ Anterior Segment Partial Coherence Interferometry
▶ Biometry, Use and Principle of

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Partial Oculocutaneous Albinism

▶ Chédiak-Higashi Syndrome

Pathologic Myopia

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Synonyms

Degenerative myopia

Definition

Myopia (shortsightedness or nearsightedness) is a refractive error where light is focused in front of the retina, instead of on retina itself, leading to blurring of distant objects.

Myopia can be classified as simple (physiologic) and pathologic (or degenerative).

Eyes with simple myopia have a refractive error of less than 6 diopters (D) and lack pathological changes, whereas eyes with pathologic myopia (PM) present a refractive error of at least 6 D and/or axial length greater than 26.5 mm in association with degenerative changes occurring especially in the posterior segment of the globe.

Etiology

The etiology of PM is still unclear, but both hereditary and environmental factors seem to play a role. It may be determined by genetic factors to a greater extent than simple myopia and the genetic profile of PM might differ from that of simple myopia.

Several evidences suggested a genetic role in myopia. Twin studies have shown high concordance for myopia. Moreover, children of myopic parents have a higher incidence of myopia and the incidence is greater if both parents suffer from myopia. Multiple loci for susceptibility to myopia have been mapped, most of which are autosomal dominant. These loci include MYP3 on 12q, MYP5 on 17q, MYP6 on 22q12, MYP7 on 11p13, MYP8 on 3q26, MYP9 on 4q12, MYP10 on 8p23, MYP11 on 4q22-q27, MYP12 on 2q37.1, MYP14 on 1p36, MYP15 on 10q21.1, MYP16 on 5p15.33-p15.2, MYP17 (formerly MYP4) on 7p15, MYP19 on 5p15.1-p13.3, and MYP20 on 13q12.12. An autosomal recessive locus, MYP18, maps to 14q21-q24. X-linked loci include MYP1 on Xq28 and MYP13 on Xq23-q25. More than 30 different genes have been linked to myopia, including PAX6, COL1A1, COL2A1, TGFB1, and TGFB2. Two recently published genome-wide association studies (GWAS), namely, CREAM and 23andMe, enrolling 45,771 patients discovered 20 novel genes associated with myopia. Furthermore, PM occurs commonly in association with Marfan, Ehlers-Danlos, Down, and Stickler syndromes.

Environmental factors include close work, emotional stress, and increasing formal education. Prolonged accommodation and intraocular pressure are suspected of influencing axial elongation in eyes with decreased scleral resistance. Many factors including scleral growth and remodeling along with vitreous synthesis might be involved in the development of myopia.

Histology

In PM, several ocular structures differ from normal eyes (e.g., sclera, choroid, Bruch's membrane, and optic nerve head). In eyes with high axial myopia, scleral thickness posterior to equator is diminished in comparison to emmetropic eyes, while anterior scleral and central corneal thickness do not seem to be dependent on axial length. Subfoveal choroidal thickness is markedly decreased in eyes with high axial lengths, decreasing by 15 μm for every −1 D change. The thickness of Bruch's membrane is preserved in patients affected by high myopia. However, Bruch's membrane, together with retinal pigment epithelium (RPE) and choriocapillaris, may be absent in the temporal optic disk border and this area has been named "parapapillary gamma zone."

Regarding optic nerve head, a positive relationship has been proved between its size and axial length above 26.5 mm or refractive error below −8 D. Interestingly, such relationship does not apply to non-highly myopic eyes. Moreover, the lamina cribrosa of eyes with PM is significantly thinner than emmetropic ones.

Epidemiology

Myopia is one of the leading causes of visual impairment in the world, especially between the ages of 20–50 years. The prevalence of myopia varies between 2% and 33%, depending on the race and age of the population analyzed. The prevalence of PM has been reported to be 1–2% of the total population of the United States, but is higher in Asia and the Middle East. According to a survey conducted on Taiwanese schoolchildren, the prevalence of myopia in urban area reaches 80–90% of students aged between 16 and 18 years, whereas 10–20% have PM.

Diagnosis

The diagnosis of PM is exquisitely clinical and it depends on the refractive status and/or axial length of the patient eye. However, different imaging modalities are extremely useful to characterize myopic complication. Mydriatic fundus examination is indispensable in order to evaluate macula, optic nerve, peripapillary area, and retinal periphery. OCT is an essential tool to identify, characterize, and stage PM complications, whereas fluorescein angiography is still the gold standard for diagnosis of many macular complications.

Clinical Presentation

Several retinal abnormalities have been recognized in PM involving macula, peripapillary area, vitreoretinal interface, peripheral retina, and optic nerve. The posterior staphyloma is a paradigmatic feature of PM, consisting of thinning and ectasia of the sclera at the posterior pole, and it can be further classified in ten subforms. Posterior staphyloma incidence increases with age, and it can be found up to 80–90% of highly myopic patients over 40 years and can be complicated by chorioretinal folds in about 1% of cases. The classification of the pathologic conditions associated with degenerative myopia includes alteration at the level of the macula, optic disk, vitreoretinal interface, and peripheral retina. Additional diseases related to PM include glaucoma and cataract.

Macula

Myopic maculopathy is a potentially sight-threatening complication, characterized by one or more of the following lesions: (i) tessellated fundus, due to the visualization of choroidal vessels through the retina; (ii) lacquer cracks, which are linear breakage of the Bruch's membrane; (iii) diffuse atrophy, caused by the diffuse pigment loss of the macular pigment epithelium; (iv) patchy atrophy, which are focal round-shaped areas of chorioretinal atrophy; (v) CNV, where choroidal neovessels spread into the retina; and (vi) macular atrophy, which is a wide area of chorioretinal atrophy. In a long-term natural history study, Hayashi and colleagues observed a disease progression in approximately 40% of the eyes enrolled with a linear progression pattern from tessellated fundus to macular atrophy. Macular involvement consists of CNV, dome-shaped macula, submacular hemorrhage, and intrachoroidal cavitation.

Choroidal Neovascularization

Choroidal neovascularization (CNV) represents a major cause of visual loss in myopic eyes. Myopic CNV prevalence has been reported to be between 5% and 10%, with subfoveal location being quite frequent, accounting for 58–74% of cases, whereas juxtafoveal CNV has been described in 32% of cases. Myopic CNVs are generally small (<1 disk area), flat, grayish, and with hyperpigmented margin. Most CNVs are less than 1,000 μ in diameter, perhaps related to the underlying attenuation of the blood supply from the thinner choroid. Moreover, myopic CNVs are type II (located in the subretinal space between the sensory retina and the retinal pigment epithelium), in most cases, as opposed to CNVs associated with age-related macular degeneration, which are mostly type I (situated in the subretinal pigment epithelium space). CNVs may occur adjacent to a lacquer crack, in an area of geographic atrophy of the retinal pigment epithelium (RPE) or in an area of generalized attenuation of RPE and choroid. Among myopic patients with preexisting CNV, more than 30% will develop CNV in the fellow eye within 8 years.

Fluorescein angiography (FA) is still the gold standard for the identification of myopic CNV and can show a pattern characterized by early hyperfluorescence, with little to moderate leakage in the late phases. Previous accounts of the natural history of myopic CNV have been conflicting because this kind of lesion has often been described as having a relatively self-limiting course in the short-term follow-up. Even though

the short-term visual prognosis may be relatively good, the long-term visual outcome is frequently poor. A recent survey showed that visual acuity does not significantly change during the first 3 years from the onset of CNV but gets worse after 5 years. Indeed, visual acuity at 5 years after the onset of CNV decreased to $\leq$20/200 in 89% of the eyes and in 96% of the eyes after 10 years. This poor long-term myopic CNV prognosis has been recently confirmed by another survey.

Dome-Shaped Macula

Dome-shaped macula is a scleral protrusion within the posterior staphyloma involving the macular region. The scleral area below the DSM exhibits focal thickness. According to a recent study comparing highly myopic eyes with and without DSM, its incidence is around 20% in PM. Moreover, patients with DSM showed younger age, better visual acuity, higher refractive error, and axial length in comparison to those without DSM. Notably, DSM can be associated with macular pigmentation, foveal or extrafoveal retinoschisis, and serous retinal detachment. Since the association with serous RD and the presence of central scotoma and metamorphopsia, the differential diagnosis between dome-shaped macula and CNV may not be straightforward.

Myopic Submacular Hemorrhage

Myopic submacular hemorrhage without CNV can be found in approximately 3% of highly myopic eyes. It seems to be caused by a small breakage of Bruch's membrane with consequent bleeding. It has been hypothesized that healing of that ruptures results in lacquer cracks. The onset of myopic submacular hemorrhage is accompanied with visual acuity (VA) reduction, which usually recovers with blood reabsorption within 6 months. However, VA cannot be entirely restored, especially in eyes with disruption of inner and outer segment junction (IS/OS) line and external limiting membrane (ELM) line.

Intrachoroidal Cavitation

Macular intrachoroidal cavitation appears as an orange-colored patchy atrophic lesion within the staphyloma. It shares similar fundoscopic and optical coherence tomography (OCT) features with peripapillary cavitation. Macular intrachoroidal cavitation is linked to a higher incidence of retinoschisis within and around the patchy atrophic area.

Optic Disk and Peripapillary Area

In a study conducted in Singapore on 359 adult patients suffering from PM, peripapillary atrophy (PPA) was the most common disk finding (81.2%), followed by tilted disk (57.4%). PPA can be differentiated on OCT images into peripheral beta zone, defined as lacking of RPE with preserved Bruch's membrane, and inner gamma zone, which involves also choroid, Bruch's membrane, and deep retinal layers. Both areas are associated with long axial length, while only beta zone is linked to glaucoma.

Retrobulbar subarachnoid space (SAS) can be identified in 90% of highly myopic eyes. SAS appears on OCT scans as a hypo-reflective triangle containing weakly hyperreflective arachnoid trabeculae with the base toward the eye neighboring the optic nerve. The enlarged SAS causes an increased pressure gradient across the lamina cribrosa and this, along with the scleral and lamina cribrosa thinning, might explain the higher glaucoma incidence in highly myopic eyes.

Peripapillary intrachoroidal cavitation, formerly known as "peripapillary detachment," is an orange-yellow lesion usually below the optic nerve, which corresponds on OCT to an intrachoroidal hypo-reflective space with normal overlying retina and RPE. The estimated prevalence in highly myopic eyes ranges from 4.9% to 16.9%. Although intrachoroidal cavitation is observed only in PM, its pathogenesis is still unclear. Interestingly, ICC is associated with optic disk tilting and posterior staphyloma but not with axial length or refractive error.

Optic nerve pits are invagination in the superior or inferior border of the papilla. Their

estimated prevalence is around 16% of highly myopic eyes, whereas they are absent in emmetropic patients. Optic nerve pits can involve the optic disk or the conus if they are inside or outside the papilla, respectively. Regarding their pathogenesis, it has been postulated that the *primum movens* is the enlargement of the optic disk and, thus, the stretching of lamina cribrosa and peripapillary sclera. Since these structures are thinned in highly myopic eyes, the stretching strength might result in the focal bowing of the lamina cribrosa, accompanied by interruption of nerve fibers above the defect. Optic nerve pits are positively correlated with refractive error, axial length, and conus area.

Vitreo-Retina Interface

Macular hole is a common complication of PM. Kobayashi and colleagues demonstrated that macular holes occur in myopic patients at a younger age compared to emmetropic ones. Due to the posterior staphyloma and chorioretinal atrophy, the biomicroscopical diagnosis of macular holes can be trivial. Interestingly, 6% of patients affected by severe myopia (< -14 D) exhibited on OCT macular holes with preserved VA (asymptomatic macular holes). During 30 months of follow-up, one out of five asymptomatic macular holes developed symptoms due to hole enlargement or retinal detachment.

Macular retinoschisis (or foveoschisis) is the splitting of the inner retinal layers at the macula. Its estimated prevalence is 9–34% of the highly myopic eyes with posterior staphyloma. Macular retinoschisis can be isolated or mostly accompanied by other macular anomalies, such as premacular structure, foveal detachment, and lamellar macular holes. OCT shows macular retinoschisis as intraretinal cysts dividing retina into a thinner outer and a thicker inner retinal layer with residual tissue interposed seen as thin hyperreflective columns. Eyes with macular retinoschisis often maintain a good VA for several years. However, association with premacular structure is linked to reduction in VA.

Several studies outlined the association between epiretinal membrane and PM. It has been suggested that ERMs are the most important PM macular change in determining VA reduction.

PM is associated with peripheral retinal degeneration (i.e., lattice degeneration), retinal tears and holes. Prevalence of lattice degeneration in PM is around 14%.

Peripheral Retina

Myopia is a well-known risk factor for rhegmatogenous retinal detachment (RD). Peripheral retina diseases and macular holes, together with early vitreous degeneration and posterior vitreous detachment, account for the higher incidence of rhegmatogenous RD in eyes with PM. The relative risk of RD in PM is increased by tenfold. According to the Eye Disease Case-Control Study Group, 55% of nontraumatic RD in eyes surgically naïve occurs in myopic eyes. The degree of myopia is correlated to the risk of RD. In addition, visual prognosis of RD is significantly worse than emmetropic eyes.

Glaucoma

Several epidemiological studies in different ethnic groups revealed that open-angle glaucoma incidence is two to four times higher in eyes with PM. However, establishing the diagnosis of glaucoma in eyes with PM can be challenging due to confounding features that can be observed also in non-glaucomatous myopic eyes (e.g., tilted disk, peripapillary atrophy, deeper excavation and reduction of retinal nerve fiber layer thickness).

Cataract

The incidence of nuclear and posterior subcapsular cataract is higher in PM. Moreover, myopic eyes require more often cataract surgery than emmetropic ones. Notably, rhegmatogenous retinal detachment following cataract extraction is more common in highly myopic eyes.

Prophylaxis

Several strategies have been proposed in order to prevent myopia onset and progression, including outdoor activities, pharmacological agents, optical intervention, contact lenses, and scleral

reinforcement. A recent meta-analysis by Sherwin and colleagues pointed out that spending time outdoor is a moderate protective factor against myopia.

Although effective in slowing the myopia progression, atropine has not spread into clinical practice because of its side effects. However, very low dosage (0.01%) of atropine seems to have a significant effect together with low incidence of rebound and side effects and rebound.

Despite contact lenses have been shown to temporarily slow myopia, their effect seems to be caused by the mechanical flattening of the cornea.

Scleral reinforcement has been proposed in patients with extremely high progressive PM. However, no rigorous trial concerning this technique has been published.

Therapy

The management of myopia aims to treat (i) visual symptoms and (ii) complications.

In order to treat visual symptoms of myopia, several strategies can be employed, including glasses, contact lenses, refractive surgery, and phakic intraocular lens (IOL) implant.

Eyeglasses are a widespread tool to correct refractive error in myopic eyes. However, patients affected by PM need very high power negative lenses, which can result in optical aberrations. At the contrary, contact lenses do not cause any aberration since the distance lens to cornea is negligible.

Refractive surgery refers to a group of procedures altering the cornea shape and curvature so that light can focus on the retina. Since refractive surgery does not interfere with axial length, it does not prevent all the clinical manifestations typical of PM. The two most used techniques are photorefractive keratectomy (PRK) and laser in situ keratomileusis (LASIK).

In phakic IOL implantation, an artificial IOL is inserted in addition to the natural lens in various positions (angle-fixed, iris-fixed, posterior chamber). The visual result is good with phakic IOL and complications are uncommon and related to IOL position and type.

As previously discussed, PM is associated with several ocular complications and their management is crucial to maintain the vision.

The management of myopic CNV has recently improved. In the past decades, laser photocoagulation has been successfully applied in extrafoveal and juxtafoveal CNV. A randomized controlled trial employing krypton red laser photocoagulation demonstrated that 40% in the treated group compared to 13% in the observed group had a visual acuity improvement of at least two lines. The CNV recurrence rate was high, reaching 31.4% of all cases, especially during the first 12 months of follow-up. Another important concern regarding the laser photocoagulation of CNV is the expansion of the atrophic scar, especially toward the myopic crescent, which occurs in 92–100% of cases and can induce a severe visual deterioration when it involves the foveal center. Laser photocoagulation was not indicated when the CNV was subfoveally located, in order to avoid damage to the foveal center. Surgical interventions consisting of CNV removal and macular translocation was reported to improve visual acuity in a variable number of patients but was burdened with an 18–57% recurrence rate, with possible expansion of RPE atrophy. The purpose of macular translocation was to displace the sensory retina originally lying over the subfoveal CNV onto a healthy RPE. Limited macular translocation had the advantage of less tissue manipulation but the disadvantage of slighter foveal displacement in comparison to macular translocation with 360° retinotomy. Overall, best long-term results could be achieved by means of macular translocation with 360° retinotomy. However, macular translocation surgery was associated with severe complications, including retinal detachment, proliferative vitreoretinopathy, macular hole, and corneal astigmatism.

VIP trials demonstrated that photodynamic therapy with verteporfin was effective in retaining quality of vision by stabilizing or improving visual acuity and contrast sensitivity. In particular, median visual acuity was stable in the verteporfin-treated group, whereas patients in the placebo group lost almost two lines after the first year of follow-up. This benefit was maintained at

24 months when the median visual acuity of the treated and the placebo patients had changed from baseline by +0.2 lines and −1.6 lines, respectively. Overall, vision turned out to have improved by at least one line from baseline at month 24 in 39% of verteporfin-treated patients, compared with 13% of controls; an improvement of at least three lines was noted in 12% of treated patients, as opposed to none in the placebo patient. Photodynamic therapy with verteporfin has also been found to be beneficial for patients presenting recurrent CNV after thermal laser treatment.

The advent of anti-vascular endothelium growth factor (VEGF) treatment has completely changed the current management of degenerative myopia-related CNV. Many studies have demonstrated clinically that an anti-VEGF approach can halt the progression of myopic CNV, prompting varying degrees of improvement in visual acuity.

The rationale behind anti-VEGF therapy is related to histopathological evidence that myopic CNV can express VEGF and that the VEGF aqueous level in eyes hosting myopic CNV can be reduced after intravitreal injection of bevacizumab. Moreover, many studies have been reported describing the positive effects of the anti-VEGF approach to CNV related to AMD on FA and optical coherence tomography (OCT). In particular, the results of the RADIANCE trial assessed both efficacy and safety of ranibizumab, administered under two different pro re nata (PRN) schedules for myopic CNV compared with vPDT.52 Patients receiving PRN ranibizumab were treated according to two criteria: visual acuity stabilization criteria (no treatment if no change in BCVA compared with two preceding monthly visits) or disease activity criteria (treatment administered if there is vision impairment attributable to intraretinal or subretinal fluid or active leakage as assessed by OCT and/or FA). The results showed that both PRN regimens of ranibizumab induced significantly greater gains in BCVA than PDT (10.5 (visual acuity stabilization criteria) and 10.6 (disease activity criteria) vs 2.2 letter change (PDT)) at month 3. By month 12, the mean changes in BCVA were 13.8 (visual acuity stabilization criteria) and 14.4 (disease activity criteria) letters for the two ranibizumab groups (with a median of 4.0 and 2.0 injections, respectively), compared with 9.3 letters for patients receiving PDT who could be switched to ranibizumab from month 3 onwards (with a median of 2.0 injections between months 3 and 12). The REPAIR trial showed eyes with myopic CNV receiving a baseline injection of ranibizumab followed by monthly monitoring and a PRN treatment regimen based on disease activity, achieved a mean BCVA gain of 13.8 letters with a median of 3.0 injections, over a 12-month follow-up.

The efficacy and safety of aflibercept for myopic CNV was evaluated in the MYRROR trial, over a 12-month follow-up. Patients received aflibercept according to a PRN schedule based on visual and anatomical criteria, and the interim 6-month results reported a 12.1-letter improvement in BCVA compared with a 2-letter loss in those receiving sham injection.

Although bevacizumab is not approved for intraocular use and evidence on its safety and efficacy profile is limited, many studies published the interesting results, with increases in visual acuity of between 4 and 18 letters after 12 months.

Although at risk for rhegmatogenous RD, laser treatment of lattice degeneration and asymptomatic retinal breaks is not currently endorsed by the scientific community due to insufficient evidences. However, laser treatment of symptomatic breaks is strongly recommended due to high incidence (35%) of RD.

The treatment of rhegmatogenous RD in myopic eyes does not significantly differ from those of non-myopic eyes and it includes PPV with gas or silicone oil tamponade, scleral buckling, pneumatic retinopexy, and combinations of above techniques. However, if a MH is associated with RD, cryotherapy, diathermy, or laser photocoagulation can be additionally performed.

Macular hole can be treated by means of numerous surgical techniques, including pars plana vitrectomy (PPV) with gas or silicone oil tamponade, episcleral posterior buckling, suprachoroidal buckling, and scleral shortening. Despite myopic refractive error does not seem to

affect the whole repair surgical outcomes, the concomitant presence of macular retinoschisis could be a poor prognostic factor for anatomical success rate and visual recovery.

Surgery of macula retinoschisis is warranted when VA is impaired. Several surgical procedures have been proposed and no standardized procedure to treat retinoschisis is currently available. However, vitrectomy with or without internal limiting membrane (ILM) peeling seems to be effective.

Epiretinal membrane surgery is indicated whether severe significant visual symptoms occur. Epiretinal membrane peeling improves VA and metamorphopsia. Notably, ERM surgery outcomes do not differ between patients with and without PM.

Prognosis

Visual prognosis is good unless one or more complications develop. If no complication occurs, visual acuity can be restored by means of eyeglasses or contact lenses; otherwise, vision can be irreversibly compromised.

Conclusion

Pathologic myopia is defined as refractive error of at least 6 D and/or axial length greater than 26.5 mm. It is associated with degenerative changes involving several ocular structures, including macula, optic nerve, peripapillary area, retinal periphery, vitreo-retinal interface and lens. Myopia therapy aims to treat visual symptoms and complications, if they occur.

Cross-References

- ▶ Cataract, Causes and Treatment
- ▶ Choroidal Neovascularization
- ▶ Epiretinal Membrane
- ▶ Macular Holes
- ▶ Refractive Surgery
- ▶ Retinal Detachment
- ▶ Retinal Peripheral Degeneration

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Paving Stone Degeneration – Cobblestone Degeneration

▶ Retinal Peripheral Degeneration

Pediatric Glaucoma

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Synonyms

Childhood glaucoma

Epidemiology

Glaucoma in the pediatric population is not common but can have devastating visual consequences. Estimates of the proportion of pediatric

glaucomas represented by congenital glaucoma have varied from 38% to 70%. In the Western world, congenital glaucoma has been reported to occur in about 1 in 10,000–30,000 births, but the incidence is greater in Saudi Arabia and areas with high rates of consanguinity. Since it has been estimated that a general ophthalmologist in the Western world may see a single case of congenital glaucoma every 5 years, this paucity of experience with the disease likely contributes to misdiagnosis and/or suboptimal treatment. This may in turn result in the occurrence of irreversible corneal and optic nerve damage prior to a correct diagnosis. Consequently, congenital glaucoma accounts for a disproportionately high proportion (up to 18%) of children in blind institutions around the world. Overall glaucoma is responsible for 5% of blindness in children worldwide.

Definition

Although there are many classification systems for the pediatric glaucomas, it is generally accepted that pediatric glaucoma is *primary* when there is an isolated developmental abnormality of the angle. Primary pediatric glaucomas include newborn primary congenital glaucoma, infantile primary congenital glaucoma, late-recognized primary congenital glaucoma, and juvenile open-angle glaucoma. Historically, the childhood glaucomas have been labeled *developmental* glaucomas based on the associated presence of developmental defects of the eye.

Etiology

The most common causes of glaucoma in the pediatric population have most consistently been reported as being primary congenital glaucoma and aphakic glaucoma. Aphakic glaucoma is a complication of pediatric lensectomy surgery and can occur following up to 41% of congenital cataract surgeries. A review of the literature suggests that aphakic glaucoma most commonly occurs several years after congenital cataract surgery, especially if the surgery was performed in the first year of life, if corneal diameters are less than 10 mm, and if there are other ocular abnormalities (Chen et al. 2004).

Clinical Presentation

Early diagnosis is the cornerstone of glaucoma management, particularly given that glaucoma is the leading cause of irreversible blindness worldwide (Tham et al. 2014). Every ophthalmologist should be familiar with the cardinal signs and symptoms of primary congenital glaucoma, which include photophobia, epiphora, and blepharospasm. Other associated signs for this disease include cloudy cornea and buphthalmos. All ophthalmologists should also be aware of the need for lifelong screening for glaucoma after congenital cataract surgery, even if the surgery is uneventful. The ocular or systemic diseases commonly associated with glaucoma should be recognized and include trauma, uveitis, anterior segment dysgenesis, aniridia, Sturge-Weber syndrome, neurofibromatosis, and persistent hyperplastic primary vitreous (or persistent fetal vasculature).

Once glaucoma is diagnosed, it is important to refer the patient to an ophthalmologist who has experience with the full range of medical and surgical treatments for the disease.

Diagnosis

Measuring intraocular pressure accurately is integral for glaucoma diagnosis. Even though Goldmann applanation tonometry represents the gold standard for pressure measurement, this method is particularly challenging in the office for both infants and young children. Perkins applanation tonometry offers another gold standard alternative that is portable and can be used in the upright and supine position, which has obvious advantages in infants. Other methods of tonometry may have pressure readings that differ from the Goldmann and Perkins devices, but these methods still have certain advantages in specific situations. For example, pneumatonometry and Tonopen devices are useful in patients with

corneal scarring and edema. Rebound technology with the iCare device affords another portable alternative which does not require topical anesthesia. Schiotz tonometry is uncommon but affords another low-cost, portable alternative.

When diagnosing buphthalmos in a newborn, it is important to remember that the normal newborn has a corneal diameter of 10 mm. When glaucoma occurs in the first 2–3 years of life, buphthalmos can occur and is often associated with Haab's striae, or Descemet's membrane breaks, which can be associated with a cloudy cornea, photophobia, epiphora, and blepharospasm. After 2–3 years of age, the corneal diameter should normally be 12 mm (Bruce 1992). Glaucoma presenting after 2–3 years of age is not usually associated with buphthalmos or cloudy corneas but instead may be relatively asymptomatic, as the eye no longer easily distends with increased intraocular pressure.

An exam under anesthesia (EUA) often affords the best opportunity for a critical examination of the eye, which should include refraction, gonioscopy, and optic nerve evaluation. Buphthalmos may be associated with axial lengths and myopia that are greater than expected for a particular patient. Notably, intraocular pressure evaluation during an EUA may be inaccurate, and every opportunity to measure the intraocular pressure in the office should be done. When planning an EUA, the doctor should be aware that intraocular pressure may increase during intubation and extubation. Inhalational anesthetics may decrease intraocular pressure, and these agents include halothane, nitrous, propofol, sevoflurane, isoflurane, and enflurane. Other medications used during an EUA may increase intraocular pressure and include ketamine, succinylcholine, and suxamethonium.

Differential Diagnosis

The differential diagnosis for epiphora includes nasolacrimal duct obstruction, conjunctivitis, and trauma. The differential diagnosis for buphthalmos includes megalocornea.

The differential diagnosis for a cloudy cornea is often best remembered by the mnemonic STUMPED. STUMPED stands for Sclerocornea, birth Trauma (with vertical breaks in Descemet's), corneal Ulcers, Mucopolysaccharidoses, Peter's anomaly, Endothelial dystrophies (e.g., CHED or congenital hereditary endothelial dystrophy), and Dermoids. Therefore, when examining a baby with cloudy cornea, one should always remember congenital glaucoma and should also never be STUMPED or at a loss in coming up with a differential diagnosis for a cloudy cornea.

An elevated intraocular pressure often distinguishes pediatric glaucoma from these other entities.

Prophylaxis

The best prophylaxis for irreversible optic nerve damage and vision loss is early diagnosis. Since one of the leading causes of vision loss in pediatric glaucoma is amblyopia, aggressive amblyopia treatment is critical in the management of these patients.

Surgically, there may be only one procedure that may decrease the chance of glaucoma development in aniridic patients. Serial gonioscopy after 1 year of age may reveal progressive aniridic angle changes, which may lead to glaucoma later in life. However, prophylactic goniosurgery to peel the iris stump away from the angle may decrease or prevent the future development of aniridic glaucoma in this select group of patients with documented progressive angle changes (Chen and Walton 1999).

Therapy

The treatment of the pediatric glaucomas is primarily surgical, because medications are often ineffective and poorly tolerated long-term in the pediatric population. For example, alpha-adrenergic agonists, such as brimonidine, can cause central nervous system depression with resultant somnolence, hypotension, bradycardia, and respiratory difficulty. Therefore, brimonidine is contraindicated in infants and should be avoided in children under the age of about

6 years. Although oral acetazolamide appears to be more effective than topical carbonic anhydrase inhibitors, systemic acetazolamide may be associated with clinically significant metabolic acidosis in infants and children. Because of their associated side effects in infants and children, intraocular pressure-lowering medications are often used as temporizing agents prior to more definitive surgical treatment.

A review of the literature suggests that goniotomy is a safe and effective procedure for the treatment of primary congenital glaucoma (Chen et al. 2014). It is also effective in cases of uveitic glaucoma, especially in children under 10 years of age and in those with minimal peripheral anterior synechiae. Trabeculotomy is also a good option for primary congenital glaucoma, especially in cases where corneal opacity precludes the ability to perform goniotomy. Both standard and suture trabeculotomy are good options in such situations. The use of an illuminated microcatheter may facilitate trabeculotomy surgery.

The literature suggests that congenital glaucoma is more common and severe in regions where consanguinity is more common relative to other regions of the world. In these cases which often present with a greater degree of corneal opacity and buphthalmos, combined trabeculotomy-trabeculectomy may result in better intraocular pressure control than angle surgery alone.

Although success rates for trabeculectomy are poor in the first year of life and in children who are aphakic, this procedure remains an option in older children and for those who have failed primary angle surgery. While the adjunctive use of mitomycin (MMC) may increase the success rate of this procedure, the results are less clear with the adjunctive use of 5-fluorouracil (5-FU). The long-term risk of bleb-related infection, which appears to be more common in children, should be considered in the surgical decision process.

Tube shunt surgery may be a good option in aphakic patients who have lower success rates with trabeculectomy and who may require contact lens wear for visual rehabilitation. Tube surgery complications that may be more common in the pediatric population include tube migration, tube erosion, and infection.

Cyclodestruction may be used in the pediatric population when other surgical modalities have failed.

Nonpenetrating deep sclerectomy surgery in the pediatric population appears to have modest success, because a significant proportion of cases are associated with an inability to find Schlemm's canal, which makes the surgery technically challenging to perform. The studies also suggest that efficacy increases with conversion to a penetrating or trabeculectomy surgery, but conversion to a trabeculectomy surgery or a penetrating surgery is associated with increased postoperative complications.

Less commonly reported procedures in the pediatric population include endoscopic goniotomy, trabeculodialysis, and trabeculopuncture.

Prognosis

Despite aggressive management, congenital glaucoma may still produce severe visual loss due to amblyopia, corneal scarring, refractive error, and/or optic nerve damage. Prognosis is optimized with early diagnosis and aggressive amblyopia management.

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Pediculosis (Lice), Ocular Infection

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Synonyms

Pediculosis ciliaris; Pediculosis palpebrarum Phthiriasis; Phthiriasis palpebrarum

Definition

An eyelash infestation most commonly due to *Phthirus pubis* (pubic lice.) *Pediculosis humanus corporis* (body lice) or *Pediculus humanus capitis* (head lice) can also cause pediculosis.

Etiology

Eyelash infestation with lice is associated with sexual transmission (pubic lice) or from direct contact with other affected individuals (body or head lice).

Clinical Presentation

Infestation of eyelashes may occur at any age, with the highest frequency noted among men between the ages of 15 and 40. Affected individuals present with pruritus, irritation, and foreign body sensation.

Slit-lamp examination reveals lice and nits visible on eyelashes and lids. Lice may be identified by a distinct appearance, with pubic lice measuring 1–2 mm in length with round, flattened, crab-like bodies and three pairs of legs; body and hair lice are elongated, measuring 2–3 mm in length with three pairs of legs anteriorly. Nits are ovoid and opaque, measuring 0.5–1 mm in size, and adherent to lashes, seen often near the base. Erythematous lesions from louse bites are seen on the lids along with reddish-brown deposits (lice feces) on lashes (Lacarrubba and Micali 2013).

Pediculosis can also present as blepharitis or a chronic, follicular conjunctivitis. Lice may also cause secondary bacterial infections.

Diagnosis

Pediculosis is diagnosed by direct observation of lice and nits on eyelashes with handlight or slit-lamp examination. Lice are more easily distinguishable with use of a Wood's lamp, which causes lice to fluoresce.

Differential Diagnosis

Chronic blepharitis and conjunctivitis with mattering of the lashes are seen in infestation with *Demodex folliculorum*. In contrast to lice, however, organisms are eight legged, transparent, 300–400 μm in size, and most easily visualized through examination of an epilated eyelash under a microscope. These mites are harbored in a majority of elderly individuals, in contrast to lice which are more prevalent among the young.

Prophylaxis

Pediculosis is spread by close personal contact or sharing of towels and bedding with an affected individual; prophylaxis is dependent on avoiding exposure. Treatment of affected partners and family members is important to avoid recurrent infestation.

Therapy

Initial, first-line therapy starts in the office with mechanical removal of lice and nits at the

slit-lamp biomicroscope using jeweler's forceps. Trimming of eyelashes may also be considered to reduce the burden of nits. However, lice and nits at the base of the lashes may be missed if mechanical treatment is utilized alone.

Medical therapy is based on a 7–10 day period of incubation and subsequent hatching of nits, with a 48 h feeding period required for survival. Treatment periods are therefore utilized for 1–2 weeks. Topical antibiotic ointment such as bacitracin or erythromycin, applied to the eyelids three times daily, may smother lice and nits. If unavailable, petroleum jelly has been reported as an alternative. While therapy with physostigmine ophthalmic ointment (0.25–1%) twice daily is directed toward the organism, successful use of pilocarpine gel (4%) has also been reported; these may be effective due to either smothering of organisms, paralysis of lice, or both. Treatment with yellow mercuric oxide (1–2%) ophthalmic ointment applied to the lashes four times daily or oral therapy with ivermectin in two doses 1 week apart are also directed toward current lice (Kumar et al. 2003).

To prevent re-infestation or to prevent spread, anti-lice shampoo and lotion for non-ocular areas and treatment of family members and sexual partners, as well as thorough washing of clothing and linens, are recommended.

Prognosis

Overall, prognosis is favorable with removal of lice and nits. Medical therapy directed toward systemic eradication of the organism and spread to others is helpful to prevent re-infestation (Rapuano 2011).

Epidemiology

Pediculosis of the eyelashes most frequently occurs from pubic lice, with infestation from body and head lice reported less frequently. Spread of pubic lice is most frequent among young and middle-age adults. Infection with head and body lice is more often reported in school-age children, particularly in areas of high population density and low socioeconomic status, associated with poor hygiene (Dunphy et al. 2007).

Cross-References

- ▶ Blepharitis
- ▶ Follicular Conjunctivitis

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Pediculosis Ciliaris

- ▶ Ocular Lice
- ▶ Pediculosis (Lice), Ocular Infection
- ▶ Phthirus Pubis (Crab/Pubic Louse), Ocular Infection

Pediculosis Palpebrarum

- ▶ Ocular Lice
- ▶ Pediculosis (Lice), Ocular Infection

Pediculosis Pubis

- ▶ Phthirus Pubis (Crab/Pubic Louse), Ocular Infection

Pedigree Analysis, Symbols Used in

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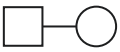
Definition

Standardized symbols used to study the inheritance patterns of a trait or disease.

	Blank circle	Female
	Filled in square or circle	Affected individual
	Square and circle connected by one line	Mating
		Offspring
	Roman numerals (I, II, II, IV)	Generations
	Arabic numerals	Birth order within generations

Purpose

These symbols are used to represent aspects of a pedigree. The pedigree is used in genetic evaluations to document the family history.

Principle

By examining an individual's family history one could determine if a disease is inherited and the mode of inheritance.

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Peduncular Hallucinosis

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Synonyms

Lhermitte peduncular hallucinosis

Definition

Peduncular hallucinosis (PH) is a rare form of complex visual hallucinations which are the result of a lesion in the ventral midbrain. PH may be continuous (lasting hours) or episodic (lasting seconds), eventually resolving, in most cases, within a few days or weeks although some cases may last longer. These hallucinations generally contain vivid imagery and might vary from one episode to the next. Some might experience multimodal hallucinations involving sound, touch,

and body posture. Most patients are able to distinguish their hallucinations from reality. PH closely resembles hallucinations caused by Charles Bonnet syndrome (release hallucinations) associated with visual loss.

Etiology

PH is a result of lesions of the midbrain usually caused by ischemic infarction involving the cerebral peduncles or reticular formation within midbrain. Thalamic infarction can also result in similar symptoms in some cases.

Clinical Presentation

PH is characterized by complex visual hallucinations which occupy the entire visual field. The patient is usually aware that he or she is hallucinating. These episodes may be continuous or episodic over the course of a few days to weeks. Related symptoms, as the result of midbrain lesions, may appear as third nerve palsy, gait ataxia, or hemiparesis.

History

The earliest postmortem reports of peduncular hallucinosis were published by Lhermitte and van Bogaert in 1922 and 1925, respectively. The first diagnosis of peduncular hallucinosis with MRI was described in 1987 by Geller and Bellur.

Diagnosis

Midbrain infraction, and diagnosis of PH, can be identified by cranial magnetic resonance imaging (MRI). Sleep-wake cycle disturbance is prevalent in the majority of cases: daytime sleepiness (diurnal somnolence) and nighttime wakefulness (nocturnal insomnia). Damage in adjacent midbrain structures may also result in unilateral or bilateral third nerve palsy, hemiparkinsonism, hemiparesis, and gait ataxia.

Differential Diagnosis

Charles Bonnet syndrome (release hallucinations) and midbrain infarction third nerve palsy

Treatment

PH caused by midbrain infarction generally subsides after a few days or weeks, though cases lasting years have also been reported. A recent case showed successful treatment of PH with an atypical antipsychotic drug (olanzapine).

Prognosis

Full recovery after a few days or weeks is expected for most patients, though some patients have reported for symptoms of PH for multiple years.

Epidemiology

Peduncular hallucinosis is a rare form of complex hallucinations, and there has been no official report of the frequency of PH in the United States or worldwide.

Cross-References

- ▶ Charles Bonnet Syndrome: Overview
- ▶ Drugs: Hallucinations
- ▶ Third Nerve Palsy

Further Reading

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PEEs

▶ Punctate Epithelial Defects/Erosions

Pegaptanib

▶ Antivascular Endothelial Growth Factor

Pelli-Robson Chart

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Synonyms

Pelli-Robson test

Definition

A test chart introduced by Denis Pelli and John Robson to determine contrast sensitivity using familiar Sloan letter optotypes rather than sinusoidal gratings (Pelli et al. 1988). The chart uses letter triplets spanning a range of 0–2.25 logCS. At the typical testing distance of 1 m, the optotype size equals 1.3 logMAR. The corresponding dominant spatial frequency of 1.5 cycles per degree is near the peak of the contrast sensitivity function for letter optotypes (Bach et al. 2008). The Pelli-Robson chart allows a quick determination of contrast thresholds at a high repeatability (Elliott and Bullimore 1993; Bühren et al. 2006) using optotypes that subjects are familiar with. Potential disadvantages are related to the large optotypes (insensitivity to subtle aberration-induced blur) and to the chart nature (probability of correct guessing, no glare source and dependence from room illumination).

Cross-References

▶ Contrast Sensitivity
▶ Sloan Letters

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Pelli-Robson Test

▶ Pelli-Robson Chart

Pellucid Corneal Marginal Degeneration

▶ Pellucid Marginal Degeneration

Pellucid Marginal Corneal Degeneration

▶ Pellucid Marginal Degeneration

Pellucid Marginal Degeneration

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Synonyms

Pellucid corneal marginal degeneration; Pellucid marginal corneal degeneration

Definition

Pellucid marginal degeneration (PMD) is a rare disorder of the peripheral cornea affecting usually the most inferior quadrant. The hallmark of this disease is the inferior corneal thinning localized 1–2 mm from the limbus.

Etiology

At present, the etiology of this disease is not known, and there is a discussion about the fact that PMD, keratoglobus, and keratoconus are different diseases or the same disorder with different clinical presentations. Lately, several authors had proposed that PMD is a peripheral form of keratoconus due to the occurrence of two diseases.

Clinical Presentation

History

Patients with PMD are asymptomatic for a long period of time except when the disease progresses. When this stage arrives, the patient complains about gradual vision decreased in spite of changing spectacles or contact lenses. This is due to the increased irregularity, against the rule astigmatism. Much less frequent can arise red eye, pain, or sudden visual acuity reduction. When this happens, it's the result of corneal hydrops or even much less frequent peripheral corneal perforation.

Physical Examination

When checking visual acuity in the early stages, the patients present with good vision, special with pinhole, even in late-stage disease due to peripheral disease. When trying to do refraction, it shows against the rule astigmatism that can be very irregular.

When examination is done with the slit lamp, PMD is characterized by 1–2 mm inferior peripheral thinning extending from 4 to 8 o'clock that spares 1–2 mm area of normal cornea between the limbus and area of thinning. The area of conical protrusion occurs above the inferior thinning. Other important aspect is that in PMD there is no Vogt's striae, no Fleischer rings, no lipid deposits, no neovascularization nor inflammation nor epithelial defects.

Diagnosis

Classical corneal topography or more recent Orbscan™ or Pentacam™ is the gold-standard diagnostic test for PMD. With the corneal topography only can surface irregularities of the cornea be evaluated, but cannot do corneal pachymetry. With Orbscan™ or Pentacam™, we can use not only the topographic maps but also the pachymetric maps and even the elevation maps. These equipment allow not only an early and subclinical detection of PMD but also the progression of this disease.

The topographic maps usually show abnormalities above the thinned zone, with flattening of the cornea along the vertical meridian with against-the-rule astigmatism. In more advance cases, the inferior peripheral steepening extends into the mid-peripheral with the inferior oblique corneal meridians in a "crab claw" or "butterfly" appearance.

The pachymetry maps are very useful in corroborating the topographic maps, because they

show the inferior corneal thinning where the steepening is maximum, which is the reverse of the typical pattern in normal corneas. So, to have more reliable diagnosis is necessary to obtain the two maps information.

Differential Diagnosis

PMD is most frequently not diagnosed because other ectatic diseases as keratoconus is more common.

Differential diagnosis included:

- Keratoconus
- Keratoglobus
- Terrien's marginal degeneration
- Mooren's ulcer
- Furrow degeneration

Therapy

Nonsurgical Methods.

The management of PMD is dependent on the stage of the disease. In very early stages are used nonsurgical methods in order to improve the visual acuity. The nonsurgical methods include:

- Spectacles
- Soft contact lens
- RGP contact lens
- Hybrid contact lens
- Scleral contact lens

The use of spectacles and soft contact lens is very reduced because it only works in the very early stages of PMD. RGP and hybrid contact lens are good options and provide a good vision; however, they can be very challenging in achieving a good fitting pattern.

Surgical Methods

As PMD progress and if nonsurgical management fails, other solutions are needed to improve patient's visual acuity, that is, methods to reduce the irregular astigmatism. Those methods are called surgical treatment of PMD, which includes:

- Cross-linking
- Intrastromal corneal segment rings
- Deep anterior lamellar keratoplasty
- Lamellar crescentic keratoplasty
- Corneal wedge excision
- Tuck-in lamellar keratoplasty
- Penetrating keratoplasty

Because PMD is so peripheral, choosing penetrating keratoplasty is very challenging due to the obligation of doing a large diameter graft (removing all peripheral thinning cornea). This technique can be more prone to rejection due to the proximity to the limbus and blood vessels. If the choice is decentered grafts, it can be associated with high astigmatism and with rejection due to the proximity to the limbus.

Some publications mentioned that doing first peripheral lamellar crescentic keratoplasty, followed by a central penetrating keratoplasty after a few months, can be a good surgical management of PMD.

Acute Management

Acute hydrops with corneal edema is a possible but rare complication of PMD. Like in keratoconus, this complication happens when there is a rupture in Descemet's membrane. PMD patients with this complication or even with peripheral corneal perforation are really ophthalmological emergencies. These two possible sight-threatening conditions can be managed with application of glue tissue adhesive, associated or not with soft contact lens, lamellar crescentic keratoplasty, or even penetrating keratoplasty.

Prognosis

PMD is a very slow progressive disease that can lead to low vision but only in the fourth or fifth life decade. The most important is to establish the correct diagnosis in order to manage this disease

with the less morbidity as possible. Neither there are no studies that show how many patients need surgical management nor even how many have sight-threatening complications as corneal perforations.

Epidemiology

PMD is a rare disease, much less common than keratoconus but more common than keratoglobus and posterior keratoconus; however, till now there are no studies about prevalence or incidence of PMD. There is no racial and no geographical predisposition. Past studies showed no sex preponderance; however, recent publications show some male predilection. Typically patients are between the age of 20 and 40 when the diagnosis is done.

Cross-References

- ▶ Corneal Astigmatism
- ▶ Keratoconus
- ▶ Lamellar Keratoplasty

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Pellucid Marginal Degeneration (PMD)

- ▶ Stromal Degenerations

Pemphigoid, Cicatricial

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Synonyms

Mucous membrane pemphigoid (MMP); Ocular cicatricial pemphigoid (OCP)

Definition

Mucous membrane pemphigoid is a chronic inflammatory disease that affects mucous membranes of the eyes, gastrointestinal system, skin, and genitals. When the eyes are involved, the term ocular cicatricial pemphigoid (OCP) is used.

Etiology

OCP is thought to represent a cytotoxic, type II hypersensitivity where autoantibodies are directed against cell surface antigens such as bullous pemphigoid antigen II (BP 180), located in the epithelial basement membrane zone (Weisenthal 2013). When these autoantigens are activated in the eye, resultant inflammation and breakdown of the conjunctival surface occur: a process termed cicatrization. IL-1, TNF-alpha, and macrophage-colony stimulating factor are all found to be overexpressed in OCP (Weisenthal 2013). When severe or left untreated, OCP can result in ocular surface scarring and vision loss.

Clinical Presentation

Ocular Manifestations

Symptoms:
Conjunctivitis, tearing, ocular irritation, burning, foreign body sensation, mucoid discharge, photophobia, and diplopia

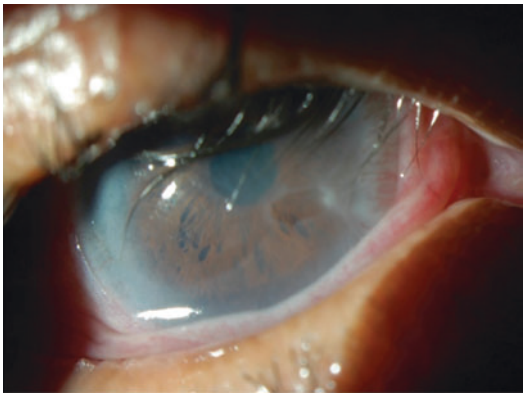
Signs:
Subepithelial fibrosis, conjunctival edema and hyperemia, conjunctival shrinkage/inferior forniceal shortening, symblephara, corneal epithelial defects or ulceration, limbal stem cell deficiency, distichiasis/trichiasis, restriction of EOM, and lagophthalmos (see Fig. 1).

Stage I: chronic conjunctivitis with subepithelial fibrosis

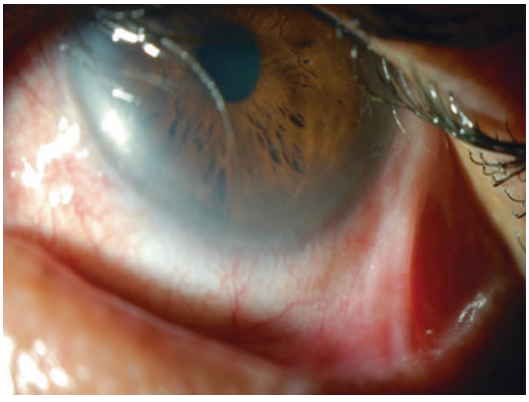
Stage II: shortening of the inferior fornix

Stage III: symblepharon formation (see Fig. 2)

Stage IV: end-stage disease manifesting as ankyloblepharon, severe sicca syndrome, and ocular surface keratinization with limbal stem cell deficiency



Pemphigoid, Cicatricial, Fig. 1 Trichiasis, corneal epithelial defects, conjunctival hyperemia, and chemosis in an OCP patient



Pemphigoid, Cicatricial, Fig. 2 Stage 3 OCP with symblepharon formation

Stage II–III subclassification: a 0–25%, b 25–50%, c 50–75%, and d 75–100% loss of inferior fornix depth

% horizontal involvement of symblephara by (X) number of symblephara

That is: OCP stage IIc IIIb(2) 50–75% loss of inferior fornix and 25–50% involvement by two symblephara

Extraocular Manifestations

Forty percent of patients may have oral involvement and include erosions of the buccal mucosa, gingiva, lip, and/or palate. Other gastrointestinal involvement includes erosions/scarring of the esophagus and anal mucosa. Twenty-five percent of patients may have skin involvement including inflammatory bullae and erosions of the head, neck, and upper trunk (Krachmer et al. 2005). Additionally, urethral and vaginal strictures can be present.

Conjunctival involvement (75%) may occur as early as 10 years before other mucosal or skin lesions develop, or it may occur as late as 20 years after the onset of other lesions (Krachmer et al. 2005).

Diagnostics

Tissue biopsy with immunohistochemical confirmation provides definitive diagnosis and should be obtained prior to institution of therapy (Krachmer et al. 2005). Biopsies can be taken from the skin, oral mucosa, or bulbar conjunctiva. Biopsies should be taken adjacent to active lesions to yield lower false negative results. If extraocular lesions are present, biopsies should first be attempted in these more accessible sites for tissue diagnosis.

Hematoxylin and Eosin

Conjunctival tissue stained with hematoxylin/eosin demonstrates squamous metaplasia with goblet cell loss (without epithelial dysplasia), subepithelial bullae, and a dense plasma cell infiltrate in the substantia propria (Rosa 2013).

Immunohistochemistry

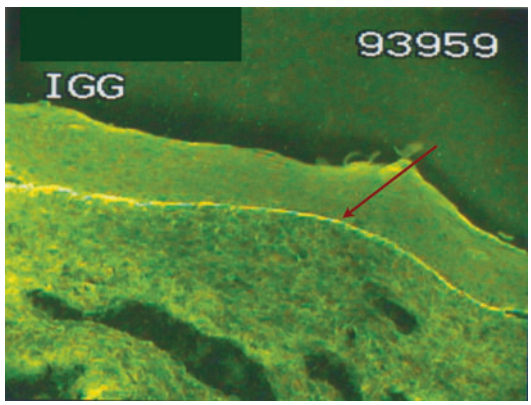
Direct immunofluorescence should be performed on all conjunctival biopsy samples. Direct immunofluorescence demonstrates characteristic linear deposition of IgG, IgA, and/or C3 along the epithelial basement membrane zone. Immunofluorescence has a diagnostic sensitivity of 50% (Rosa 2013) (see Fig. 3).

Differential Diagnosis

Other diagnostic considerations include any disease process that can cause a cicatrizing conjunctivitis:

> Allergic causes include →atopic keratoconjunctivitis and →toxic epidermal necrolysis/Stevens-Johnson syndrome. Autoimmune causes include sjogren's syndrome, lichen planus, linear IgA bullous disease, →sarcoidosis, systemic lupus erythematosus, and scleroderma. Toxic causes include pseudopemphigoid (medicamentosa). Neoplastic causes include conjunctival sebaceous cell carcinoma or damage from ionizing radiation. Sequelae of infectious etiology include trachoma, adenovirus conjunvitivits, and corynebacterium diphtheria conjunctivitis.

Pseudopemphigoid is associated with use of various medications such as sulfa antibiotics, penicillin, phenytoin, topical pilocarpine, epinephrine, timolol, idoxuridine, echothiophate, and demecarium bromide (Weisenthal 2013). In contrast to OCP, symptoms resolve once the offending medication is discontinued.



Pemphigoid, Cicatricial, Fig. 3 Conjunctival specimen in a patient with OCP. Direct immunofluorescence demonstrates heavy linear deposition of IgG and C3 along the epithelial BMZ (*arrow*). Biopsy was negative for IgA, IgM, and fibrin

Prophylaxis

No known prophylaxis has been established to prevent disease onset.

Therapy

The primary goal of treatment is the prevention of corneal scarring and vision loss. Management is often co-managed by other specialists, such as a gastroenterologist, dentist, dermatologist, etc., when extraocular involvement is present.

Medical

Medical management includes ocular surface lubrication and antibiotic ointments to prevent infectious keratitis. Long-term management typically requires systemic immunosuppressive therapy for active disease. Blepharitis and dry eye syndrome are also treated with vigorous warm compresses, punctual occlusion, and doxycycline as needed (Krachmer et al. 2005).

Systemic

Various systemic immunosuppressive medications have been used to treat OCP. Immunomodulatory therapy is typically maintained for at least 1 year with a goal of complete resolution of all conjunctival inflammation. Systemic steroids may be used for 8–12 weeks with a taper once immunomodulatory therapy becomes effective (Krachmer et al. 2005).

Dapsone 2 mg/kg/day × 12 weeks has been shown to be 70% successful in stage III OCP patients and is used for less active cases of OCP (Krachmer et al. 2005; Foster et al. 2013). Important side effects to monitor for include G6PD deficiency and hemolytic anemia.

Cyclophosphamide 2 mg/kg/day is the treatment of choice for severe OCP. Weekly CBCs are used to monitor for leukopenia for 3 months upon starting cyclophosphamide.

Azathioprine 2 mg/kg/day has been used in patients who fail dapsone (or other agents) with resolution in roughly half of cases (Krachmer et al. 2005; Foster et al. 2013). CBCs are used to monitor for bone marrow suppression.

Methotrexate and mycophenolate mofetil have been used for alternative or step-down therapies with some success when other treatments are unresponsive.

Surgical

Many patients with OCP will develop cicatricial entropion, which contributes to ocular surface disease. Epilation and/or quickert everting sutures can be performed for temporary relief of trichiasis/entropion prior to more long-term surgical options for entropion repair such as Weis procedure, tarsal fracturing, transmarginal rotation procedure, and anterior lamellar recession. Amniotic membrane transplantation or mucous membrane transplants can be used for forniceal reconstruction in stage II or worse OCP. Limbal stem cell transplant and/or penetrating keratoplasty may be needed for severe cases. Surgical procedures are best performed when the active inflammatory condition has been quiescent for a period of time to best achieve success and avoid excessive scarring/failure (Krachmer et al. 2005).

Prognosis

Prolonged periods of remission of active OCP occur in approximately 33% of patients. Remission periods last on average 34 months (Foster et al. 2013) Ongoing follow-up, even after remission, is recommended given the chronic, relapsing nature of OCP.

Epidemiology

Incidence is estimated to be between 1:8,000 and 1:46,000 ophthalmic patients (Krachmer et al. 2005). The average age of diagnosis is between the ages of 60 and 70 (Krachmer et al. 2005). Insidious onset and smoldering of symptoms can delay diagnosis of actual disease onset. Like other autoimmune disorders, OCP has a higher predisposition to affect women more than men with a 2:1 ratio (Weisenthal 2013). Occurrences of OCP in patients younger than 30 are rare. OCP can affect all races.

Cross-References

- ▶ Amniotic Membrane Transplantation Nonpharmacotherapy
- ▶ Keratoconjunctivitis: Overview
- ▶ Sarcoidosis
- ▶ Stevens Johnson Syndrome
- ▶ Symblepharon
- ▶ Trachoma

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Penetrating Eyelid Injuries

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Synonyms

Avulsion; Laceration

Definition

Partial or full thickness penetration of the eyelid and ocular adnexal structures.

Etiology

Penetrating eyelid injury may result from causes such as a motor vehicle accident, assault with a sharp object, or a fall (Nerad 2001). Lacerating trauma to the eyelid may also be seen in the context of a bite injury (see Fig. 1a, b).

Clinical Presentation

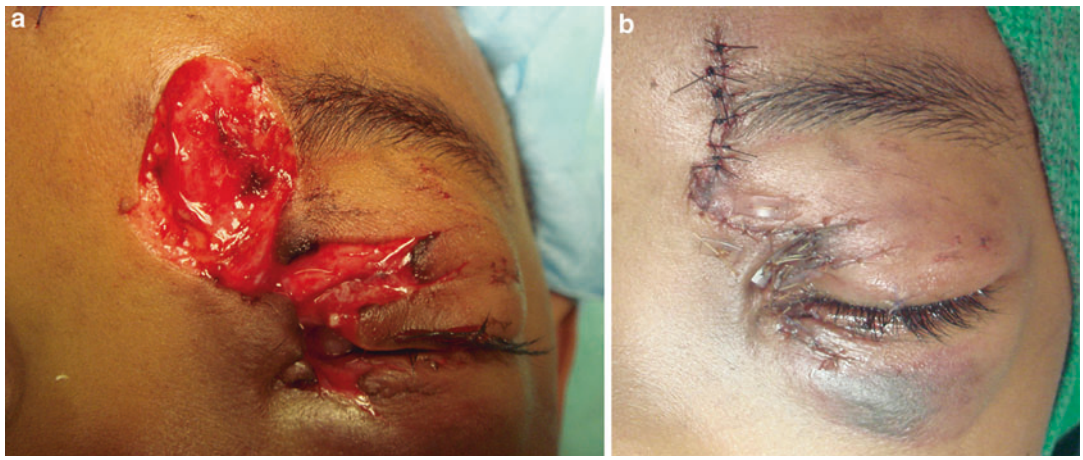
Penetration of the eyelid can be an isolated incident but most often occurs in the setting of multisystem trauma. The physician's primary role is to rule out life-threatening injury and to stabilize the patient. Sight-threatening injuries should then be addressed. The eyelid wound is explored to identify injured anatomic structures and the extent of damage. Fat present in the wound implies violation of the orbital septum and consequently, damage to the levator palpebrae superioris muscle is suspected. Full thickness eyelid trauma increases initial suspicion of globe injury. Tissue loss in the context of eyelid laceration is unusual, whereas shrinkage of tissue is more common (Weiner and Bedrossian 2002). Full thickness laceration can cause canthal avulsion, although this is more commonly seen following blunt trauma. With any penetrating injury to the medial aspect of the upper or lower eyelid, the ophthalmic examination should inspect for canalicular involvement. Additionally, penetrating injuries may leave foreign bodies in the eyelid or orbit.

Diagnostics

Examination of the patient's eye precedes examination of the eyelid. Following the eye exam, a thorough clinical examination via direct inspection of the wound is the physician's most important tool to determine the location, extent, and severity of the penetrating injury. A suspicion of a foreign body in the wound warrants imaging of the region. CT scanning of the orbit is the first line imaging protocol. If the medial aspect of the eyelid is involved, the canalicular system is inspected by careful probing. Damage to the levator is suspected when orbital fat is present within the wound and can be evaluated by measuring the levator excursion of the upper eyelid.

Differential Diagnosis

Trauma to the orbit, periocular trauma, ruptured globe.



Penetrating Eyelid Injuries, Fig. 1 (**a**) Preoperative photograph of patient status post dog bite injury with lacerations to the brow, upper eyelid, lower eyelid, and canalicular system. (**b**) Immediate postoperative photograph of penetrating dog bite injury

Prophylaxis

Penetrating injury to the eyelid can be prevented by the use of protective eyewear and polycarbonate eye glasses.

Therapy

The goal of treatment is to return normal function and cosmesis to the eyelid. Trauma to the eyelid should be repaired within 48–72 h following injury. The well-vascularized eyelid allows for somewhat delayed closure as it is at lower risk for infection. Some clinicians utilize broad spectrum oral antibiotics until wound treatment is initiated. This is particularly important in animal and human bite wounds. A general medical history should include inquiry regarding recent tetanus injections. Repair of the wound involves reapproximating tissues to their appropriate anatomic locations. If the levator muscle is found to be damaged, it is sutured back to its original location along the anterior border of the tarsus. If canalicular trauma is involved, repair can be accomplished at the same time as tissue repair. Medial or lateral canthal tendon avulsions are repaired by reinserting the appropriate limb of the canthal tendon to its bony insertion.

Prognosis

Given the highly vascular nature of the eyelid, wounds heal with minimal scarring and eyelid asymmetry. Full thickness eyelid injuries that affect the eyelid retractors may result in blepharoptosis. If the penetrating injury occurs along the lid margin, notching or asymmetry can manifest. Penetrating injuries may also cause retraction of the upper or lower eyelid secondary to fibrotic changes.

Epidemiology

Eyelid injury predominantly occurs in males aged 20–30 (Savar et al. 2008).

Cross-References

- ▶ Trauma, Canalicular
- ▶ Eyelid Trauma
- ▶ Open Globe
- ▶ Orbital Floor Fracture
- ▶ Orbital Pain
- ▶ Trauma, Lacrimal Sac and Nasolacrimal Duct

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Penetrating Injuries

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Synonyms

Perforating ocular laceration

Definition

Penetrating eye injuries refer to a full-thickness wound, with or without an exit wound. It may be associated with a retained foreign body intraocularly.

Etiology

Penetrating injuries are usually caused by sharp objects that enter the globe.

Clinical Presentation

Penetrating ocular lacerations can be divided into three categories: (1) injuries in which the offending object was immediately removed prior to presentation and in which there is no retained foreign body, (2) injuries caused by objects that pass completely through the globe that are then withdrawn (such as from a needle) without a retained foreign body, and (3) injuries in which a foreign body is retained completely or partially inside the globe.

Diagnosis

Initial diagnosis is often made on the basis of the history, which must be taken carefully and completely even if the patient does not report on suspect a penetrating ocular trauma. Many case reports have indicated that in circumstances in which there was metal work performed, penetrating ocular injuries (from filings or small fragments) must be suspected. Patients should be asked about changes in vision, foreign body sensation, or any sensation that suggests surface abnormalities of the globe or corneal abrasion. Clinical signs include conjunctival hyperemia or an obvious foreign object, though hemorrhage of the conjunctiva or subconjunctiva might obfuscate any direct visualization. Corneal abrasion may be visible on ophthalmic exam; signs include vertical abrasions that are specific for retained foreign bodies on the superior tarsal conjunctiva under the upper lid. A complete examination of *both* eyes is warranted, as injury to one should indicate the possibility of injury to the other. The lid should be everted and a dilated fundoscopic exam performed, as well as evaluations with a slit lamp exam, anterior chambers, and lens clarity. Plain radiography may be employed when a foreign body is suspected to have been retained and often will require surgical removal, though CT scan is preferred to determine the degree of ocular damage. After imaging, exploration under anesthesia should be undertaken urgently, by opening the conjunctiva and detaching of the rectus muscles. The wound, once identified, should be exposed, and displaced or damaged tissue should be noted (Kanski et al. 1999).

Differential Diagnosis

Penetrating injuries can be divided into several classes based on the depth and extent of the trauma. Corneal wounds with an intact anterior chamber may not require any surgical intervention as they will self-seal with or without a bandage contact lens. If corneal damage is suspected, a stromal infiltrate usually appears if a foreign body has been present for more than 24 hours. If the foreign body is organic (such as wood), microbial keratitis must be suspected, and in the case of metal (especially iron), foreign bodies are seen as rust-colored circular opacities on slit lamp examination. In instances in which the anterior chamber appears compromised, a dense cellular reaction is indicative of microbial ulceration of the cornea and secondary endophthalmitis. The degree of lens damage (if any), anterior/posterior scleral laceration, and retinal damage or detachment should be ascertained. For foreign bodies that are deep, the Seidel test should be performed. In the Seidel test cobalt-blue filter on the slit lamp is used to observe the area of suspected injury. A local anesthetic is placed on the eye and on a fluorescein strip which is applied to the area of injury. Since the pH of the anterior chamber is different from the surface, leaking aqueous fluid dilutes the dye on the strip (Gersenblith and Rabinowitz 2012).

Prophylaxis

Prevention of penetrating ocular trauma requires protective eye- or face wear during high-risk activities. As soon as a laceration is ascertained, the injured eye should be protected and the risk of comorbid symptoms reduced (i.e., pain, swelling, and possible associated vomiting mitigated with analgesics and/or anti-emetics). Tetanus immunization status should be elicited in the initial history taking. Corneal wounds that are left to heal spontaneously require topical antibiotics (such as

polymyxin B/bacitracin twice or thrice daily for up to 1 week). Broad spectrum antibiotics should be administered perioperatively intravenously and intravitreally to prevent endophthalmitis. A topical steroid and a mydriatic may be needed in the case of traumatic iritis. In the case of extensive damage to the globe, enucleation is advised to prevent sympathetic ophthalmia. If the damaged eye demonstrates no perception of light after suture repair within 10 days, then enucleation should be considered to prevent sympathetic ophthalmia, as well (Kuhn 2008).

Therapy

For small lacerations without a foreign body, self-healing with topical antibiotics (as indicated above) is sufficient. However, for larger and deeper lacerations (greater than 1 cm across), sutures are required to close. For corneal lacerations, the depth and number of the penetration(s) should be noted, as undue exploration for deep foreign material may exacerbate scarring. These lacerations are usually closed using nylon sutures with buried knots, and the repair should make the wound watertight. Corneal rust rings may be removed with an ophthalmic burr. For penetrating injuries that have resulted in scleral laceration, uveal or vitreous prolapse can occur through the wound. In this case, they are fully exposed with the aim of repositioning them within the globe. In many cases of corneal or scleral injury, the lens capsule is damaged, leading to hydration of the lens that ultimately causes marked intraocular inflammation. Usually, a second operation is needed to aspirate the lens or to determine whether further surgery is required on the retina (as there will be better visualization of the anterior chamber) (Probst et al. 2012).

Prognosis

Prognosis is highly dependent on the (1) severity of the injury and (2) the immediacy and completeness of evaluation and treatment. Frequent follow-up diminishes the risk of postoperative infections and complications, as well as allowing for reexamination to determine if further repair is needed. If the lens is completely damaged by the time of a second operation, the insertion of an intraocular lens (IOL) depends upon whether enough of the posterior capsule has been retained and how much iris has been retained (Kuhn 2008).

Epidemiology

Penetrating injuries are three times as common in males than in females, and over half of the injuries occur in adolescents and young adults. This is likely due to the fact that three main causes are assault, occupational accidents (e.g., working underneath a car or in a machine shop, doing woodwork, and fishing), and injuries occurring in sports. In the case of high-velocity impact injuries or injuries involving larger objects, there are often associated eyelid lacerations, which indicate the possibility of injury to the globe (Gerstenblith and Rabinowitz 2012).

Cross-References

- ▶ Intraorbital Foreign Body (IOFB)
- ▶ Orbital Hemorrhages
- ▶ Penetrating Eyelid Injuries

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Perennial Allergic Conjunctivitis

► Allergic Conjunctivitis

Perfect Capsule Device

► Sealed Capsule Irrigation Device

Perfluorocarbon

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Synonyms

Perfluorocarbon liquid (PFCL); Perfluorodecalin (C10F18); Perfluoro-n-octane; Perfluoron; Perfluorophenanthrene; Vitreon; Vitreous substitute

Definition

PFCL is a synthetic fluorinated hydrocarbon containing carbon–fluorine bonds. Some also contain other elements such as hydrogen, bromide, and nitrogen. It is commonly used as an intraoperative tool to assist the manipulation of the retina, particularly in complicated retinal detachments. In general, all PFCLs are odorless and colorless, have low viscosity, and have higher specific gravity and density than water.

A few low-density PFCLs have been investigated for potential use in ophthalmology. Of these perfluorodecalin (C10F18) was found to possess higher efficacy and was approved by the United States Food and Drug Administration for intraocular use. In the United States, perfluoro-n-octane is available as Perfluoron and perfluorophenanthrene is available as Vitreon. In Europe there are many brands of perfluorodecalin as well as perfluoro-n-octane marketed for intraocular surgery.

Indication

The main clinical indications for the intraocular use of perfluorocarbon liquids are detachments with giant retinal tears, detachments with complicated proliferative vitreoretinopathy (PVR), traumatic retinal detachments, removal of posterior lens fragments and posteriorly dislocated intraocular lenses, drainage of suprachoroidal blood, and macular rotation with a 360° retinotomy.

PFCL has also been reported to be useful in the retinal detachment associated with diabetic retinopathy, detachment associated with disk coloboma, detachment from retinopathy of prematurity, vitrectomy for endophthalmitis, displacement of submacular hemorrhage during surgical drainage, and excision of subretinal membranes. Surgical principles are the same. It helps stabilize the retina, displaces subretinal blood, reveals preretinal membranes, and assists drainage of subretinal fluid (SRF).

Contraindication

If a large posterior hole is present, perfluorocarbon liquid should not be used because there is a high probability of it going into the subretinal space.

Techniques and Principles

PFCL is a popular surgical tool due to several advantages: (1) its optical clarity allows manipulations under PFCL; (2) its high density and specific gravity allow flattening of the retina and unrolling of folds and also avoid the need for a posterior retinotomy to drain subretinal fluid (SRF); (3) it has different refractive indexes from saline enabling a visible PFCL-fluid interface, which aids intraocular maneuvers and its final removal; (4) it has a higher boiling point than water and no interference to laser wavelengths allowing endophotocoagulation under PFCL; (5) it has low surface tension and high interfacial tension which tend to hold it as a continuous bubble and reduce the risk of PFCL migration into subretinal space through the break; (6) its low viscosity allows easy injection and aspiration even with small gauge vitrectomies; (7) its immiscibility with water resists infiltration by saline and blood and allows a clear operating field despite intraoperative bleeding; (8) its immiscibility with silicone oil (SO) allows PFCL–SO exchange, which is helpful when treating giant retinal tears by reducing risk of slippage.

The majority of researchers at this time recommend the use of PFCL only as an intraoperative tool. Nevertheless some researchers have reported its safe use for short-term postoperative internal tamponade. In all cases, after PFCL has served its function, it should be removed completely from the vitreous cavity. Depending on the indication of PFCL use, PFCL–fluid, PFCL–air, or PFCL–SO exchange could be performed.

The general technique for the use of PFCL is as follows. Complete peripheral vitrectomy and at least initial removal of posterior retinal membranes are performed. The PFCL is injected with a blunt needle over the optic nerve head, flattening the posterior retina. The fluid is slowly injected, being careful to keep the tip of the injection cannula within the initial PFCL bubble to prevent fish-egging at the time of injection. The fluid is injected up to the level of the most posterior break. Membrane dissection and relief of traction are performed to assist in displacing posterior subretinal fluid or blood anteriorly. If traction has not been completely cleared and injection was too forceful, PFCL may go through breaks into the subretinal space. Fluid–air exchange is performed to allow residual subretinal fluid trapped anteriorly to drain through the break. As the air–fluid exchange continues, the blunt needle is allowed to passively PFCL until a thin layer remains on the retina. From 0.5 to 1 mL of BSS is then injected into the eye. The PFCL develops small droplets in the saline phase and can be identified and removed easily. BSS is then removed, leaving the retina flattened under air. Laser or cryopexy may then be administered. Final vitreous substitution is performed with air, gas, or SO injection. Direct PFCL–SO exchange may also be performed. As SO is lighter than PFCL, it floats on top of PFCL and fills the eye from anterior to posterior in parallel to PFCL passive aspiration.

The use of PFCL has allowed a rational method of reattaching giant retinal tears in the supine position. The high specific gravity of the PFCL creates a tamponade at the posterior edge of the break, allowing laser treatment before fluid–air exchange or fluid–SO exchange. This substantially reduces the rate of posterior slippage.

The use of PFCL has also changed the management of PVR. Before the introduction of PFCL, PVR would be dealt with from anterior to posterior. After PFCL was introduced, dissection of membranes starting from the posterior pole was made possible. This is a safer approach as it reduces the risk of iatrogenic tears and the trauma to the retina.

PFCL offers several advantages for addressing the challenges of surgical management of traumatic retinal detachment: (1) it helps stabilize the retina during vitrectomy; (2) it assists in separating the posterior hyaloid and retina; (3) it displaces preretinal, subretinal, or suprachoroidal blood; (4) it assists in the removal of incarcerated vitreous or the retina; (5) it assists in the removal of dislocated lens, intraocular lens implant (IOL), or intraocular foreign bodies (IOFB); (6) it maintains a clear media for visualization.

PFCL facilitates removal of dislocated lens, as it can be used to float the lens fragment away from the surface of the retina. This allows easier manipulation of the lens fragment during phacofragmentation and reduces the risk of injuring the retina. It is particularly useful when the dropped lens is associated with retinal detachment, where subretinal migration of fragments is prevented.

Macular rotation with a 360° retinotomy depends on PFCL, followed by liquid–SO exchange to attach the retina. Macular rotation is a surgical procedure to treat macular degeneration with subfoveolar involvement by detaching the entire retina so as to move the fovea to a position with underlying retinal pigmented epithelium that is not involved by exudative or atrophic macular degeneration. If the macular rotation is successful, counterrotation of the globe with muscle surgery is required to avoid diplopia and cyclotropia.

Outcome

The advent of PFCL technique in the surgical repair of giant retinal tears hugely improved the anatomical success rate to over 88%, even without the use of a scleral buckle.

The success rate for severe PVR has been reported to range from 84% to 96%. PFCL use also shortens operative time and allows more thorough removal of membranes.

In one series of 14 patients with detachment arising from penetrating ocular trauma, all retinas flattened intraoperatively with the use of PFCL without retinotomy. Factors associated with a lower long-term success rate were patients younger than 20 years of age, patients with previous vitrectomy, patients with a posterior retinal injury site, and patients with subretinal hemorrhage for more than 2 weeks.

Complications

Toxicity from extended intraocular use has been reported in animal as well as human reports. Toxicity to ocular tissues may be chemical or mechanical. Most toxicities are related to incomplete removal of PFCL at the end of surgery.

During surgery, predisposing factors for PFCL going under the retina include: (1) PFCL breaking into droplets, (2) giant retinal tears, and (3) incomplete relief of tractional membranes on the retina. If PFCL has accidentally penetrated under the retina, it should be removed, as it may over time migrate under the fovea, may reduce retinal function, and may cause central scotomas. Retinal hole formation has also been reported in long-standing subretinal PFCL. Even in case that subretinal PFCL is noticed postoperatively, it should be drained, as retinal sensitivity is regained after PFCL drainage.

If PFCL enters the anterior chamber, it may cause visual disturbance, corneal endothelial loss, as well as rise in intraocular pressure (IOP). Pupil block glaucoma has also been reported following the use of PFCL. PFCL removal is indicated under these circumstances and can be done at the slit lamp.

Cross-References

- ▶ Retinal Tears
- ▶ Retinal Detachment

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Perfluorocarbon Liquid (PFCL)

► Perfluorocarbon

Perfluorodecalin (C10F18)

► Perfluorocarbon

Perfluoroethane (C2F6)

► Intraocular Gases

Perfluoron

► Perfluorocarbon

Perfluoro-n-Octane

► Perfluorocarbon

Perfluorophenanthrene

► Perfluorocarbon

Perfluoropropane (C3F8)

► Intraocular Gases

Perforating Ocular Laceration

► Penetrating Injuries

Peribulbar Anesthesia

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Synonyms

Extraconal anesthesia; Parabulbar anesthesia

Definition

Percutaneous application of anesthetics into the extraconal space of the orbit.

Epidemiology

Peribulbar anesthesia (PBA) is used by a large number of surgeons as it combines low incidence of complications during anesthesia with a relatively good motor block (Alhassan et al. 2008). It is especially used in cataract surgery.

History

Development and acceptance of peribulbar anesthesia is closely related to development of cataract surgery. While in earlier times of cataract surgery, large incisions at the sclerolimbal region were necessary, full anesthesia or retrobulbar anesthesia was anesthetic mode of choice. With development of phacoemulsification, clear cornea incision, and small incision cataract surgery, the trauma and discomfort during cataract surgery became less severe; thus other techniques of anesthesia became more accepted.

Clinical Features

As PBA presents a needle block, all needles may be used; however, in order to avoid injury of the

globe, blunt needles are preferred. The reasons for this technique are a reduced risk of causing injury to the intraconal structures. The volume of anesthetic applied in PBA is higher than in retrobulbar anesthesia (RBA) (up to 12 ml) (Nouvellon et al. 2010). However, the onset of motor block after PBA may take longer than after (RBA). For cataract surgery, a sufficient motor block with anesthesia is achieved within 5 min in 85%. There are several techniques and various entry sites for PBA. A single injection technique with the least risk of injury has to be distinguished from a several injection technique at several sites. However, the nasal superior peribulbar space should be avoided as the extraconal space is narrow at this location (Nouvellon et al. 2010). The injection depth should be limited as in deeper orbit, the space between extraocular muscles and orbit wall becomes virtual.

Tests

Several test have shown that risk of injury to globe and other structures is lesser in PBA than in RBA; however, onset of motor block has been shown to take longer in BPA.

Differential Diagnosis

Retrobulbar anesthesia (RBA), intraconal anesthesia

Etiology

The term "peribulbar anesthesia" is self-explaining.

Treatment

See also "Clinical Features." Injection sites for PBA may be medial canthus, lacrimal caruncle, seminularis fold of the conjunctiva and temporal inferior.

Cross-References

▶ Cataract Surgery
▶ Topical Anesthesia

References

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Periocular Injection of Ocular Drugs

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Indication

Periocular injections are used for regional anesthesia and akinesia (lidocaine), blepharospasm and hemifacial spasm (botulinum toxin), and chemoreduction of tumor (topotecan and carboplatin), to induce ptosis in cases of corneal exposure, for the treatment of strabismus (botulinum toxin), and for the treatment of cystoid macular edema and unresponsive uveitis (triamcinolone acetonide).

Adverse Effects

Injections in the retrobulbar space carry a risk of hemorrhage especially in patients using anticoagulation therapy. Retrobulbar hemorrhages can lead to permanent visual loss due to ischemia. Increased intraorbital pressure compresses the ciliary arteries supplying the optic nerve.

Periocular injections of botulinum toxin can lead to transient blepharoptosis, ectropion, lagophthalmos, and strabismus.

Triamcinolone can increase intraocular pressure when injected in the subtenon space. Intralesional triamcinolone used in darkly pigmented patients can cause depigmentation of the overlying skin.

Perioperative PION

► Posterior Ischemic Optic Neuropathy

Periorbital Cellulitis

► Cellulitis, Preseptal, *Haemophilus* Causing

Peripheral Corneal Guttata (Hassall-Henle Bodies/Warts)

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Synonyms

Hassall-Henle bodies; Hassall-Henle warts

Definition

Peripheral corneal guttata are hyaline-filled excrescences of Descemet's membrane that occur in the peripheral cornea. These guttata are associated with normal aging. Corneal guttata that occur in the central cornea are pathologic, such as seen with Fuch's dystrophy, fleck dystrophy, corneal degenerations, or long-standing inflammatory disorders.

Corneal guttata may be associated with impaired endothelial function and may consequently disrupt the deturgescent activity of the endothelium, resulting in corneal edema.

On examination with specular microscopy, guttata appear as dark small spots on the endothelium. Histologically, they resemble mushroom caps sitting on the endothelium.

Etiology

The dysfunctional overproduction of hyaline basement membrane by endothelial cells results in the formation of corneal guttata.

Occurrence

Hassall-Henle bodies normally occur in the peripheral cornea in adults older than 25 and become more common with age.

Classification

Non-pathologic anatomic finding

Cross-References

► Corneal Degenerations
► Fuchs' Dystrophy Disease

Further Reading

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Peripheral Corneal Relaxing Incisions

► Limbal Relaxing Incisions

Peripheral Hypertrophic Subepithelial Corneal Degeneration

► Subepithelial Corneal Degenerations

Peripheral Keratitis

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Definition

Peripheral keratitis is inflammation of the outermost part of the cornea. The cornea can be divided topographically into central and peripheral portions. In the outermost portion, the peripheral cornea, the tissue begins to transition to conjunctival, episcleral, and scleral tissue. Due to the proximity of the peripheral cornea to these tissues, it is more susceptible to some disorders that do not typically affect the central portion.

Cross-References

- ▶ Cogan Syndrome
- ▶ Cornea
- ▶ Corneal Limbus
- ▶ Corneal Ulcers
- ▶ Keratitis
- ▶ Mooren Ulcer
- ▶ Terrien Marginal Degeneration
- ▶ Ulcerative Keratitis Disease

Peripheral Retina

- ▶ Ora Serrata

Peripheral Ulcerative Keratitis

- ▶ Keratolysis (Corneal Melting), Marginal, Systemic Immune-Mediated Disease

Persistent Fetal Vasculature (PFV)

- ▶ Persistent Hyperplastic Primary Vitreous

Persistent Hyaloid Artery

- ▶ Bergmeister's Papilla

Persistent Hyperplastic Primary Vitreous

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Synonyms

Persistent fetal vasculature (PFV); Persistent posterior fetal fibrovascular sheath of the lens; Persistent tunica vasculosa lentis

Definition

Persistent hyperplastic primary vitreous (PHPV) is a congenital anomaly of the eye in which there is failure of regression of the fetal primary vitreous and hyaloid vasculature. The etiology of this abnormal persistence is unknown. Most cases are seen in normal, full-term infants without other systemic findings and are unilateral.

PHPV can be further classified into three different subtypes depending on location of the persistent fetal vasculature:

1. Anterior PHPV – Retrolental fibrovascular opacities, elongated ciliary processes, cataract, and microphthalmia.
2. Posterior PHPV – Vitreous membrane or stalk from optic nerve head, retinal folds or

dysplasia, tractional retinal detachment, and optic nerve hypoplasia.
3. Combination of anterior and posterior PHPV – Most common. Findings of both anterior and posterior PHPV are present.

Etiology

In normal embryological development of the eye, the primary vitreous forms around the seventh week and begins to regress around the twentieth week of fetal development. By birth, normally all remnants of the primary vitreous and hyaloid vasculature have regressed. In PHPV, there is failure of this regression. The etiology leading to this persistence of fetal primary vitreous and hyaloid vasculature is not known. Although some reports exist describing associations with systemic or neurological diseases, most patients with PHPV are healthy, full-term infants with no other systemic problems.

Clinical Presentation

Findings of PHPV are present at birth and may be identified at the newborn exam. Patients with more posterior PHPV may not be identified until later in childhood when other visual symptoms are noted. Patients may be found to have glaucoma, strabismus, or leukocoria. Possible findings associated with PHPV include microphthalmia, cataract, retrolental plaques, shallow anterior chamber, elongated ciliary processes, persistent hyaloid artery, retinal or optic nerve dysplasia, macular abnormalities, vitreoretinal adhesions, and retinal detachment.

Diagnosis

Diagnosis is based on clinical exam findings, exams done under anesthesia, and augmented by other imaging modalities. PHPV can be visualized by ultrasound (A-scan and B-scan), computer tomography (CT), and magnetic resonance imaging (MRI). Additionally, visual evoked potentials (VEP) may be helpful to assess vision potential.

Differential Diagnosis

PHPV must be differentiated from other causes of leukocoria such as congenital cataract, retinoblastoma, Coat's disease, toxocariasis, retinopathy of prematurity (ROP), retinal astrocytomas, Norrie's disease, familial exudative vitreoretinopathy (FEVR), and other causes of retinal detachments.

Prophylaxis

None. PHPV occurs most commonly in otherwise healthy, normal infants

Therapy

Treatment of PHPV varies with the extent of findings associated with PHPV. The treatment spectrum spans from conservative observation to surgical management. Surgical intervention is aimed at improvement in visual acuity and should be performed early to increase likelihood of useful vision. Many surgical strategies are described in the literature and continue to evolve with advances in surgical technique and instrumentation. Most include a vitrectomy with or without a combined lensectomy. Aggressive amblyopia treatment is necessary postoperatively.

Prognosis

Prognosis is very dependent on the type and extent of PHPV and on the timing of diagnosis. Patients with purely anterior PHPV have a better prognosis than those with combined or posterior PHPV.

Epidemiology

PHPV is isolated and sporadic. Epidemiologic data is poor.

Cross-References

► Vitreous Humor

Further Reading

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Persistent Posterior Fetal Fibrovascular Sheath of the Lens

► Persistent Hyperplastic Primary Vitreous

Persistent Pupillary Membrane

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Synonyms

Hyperplastic persistent pupillary membrane. (Some authors consider these to be different than persistent pupillary membranes. See Clinical Relevance below.)

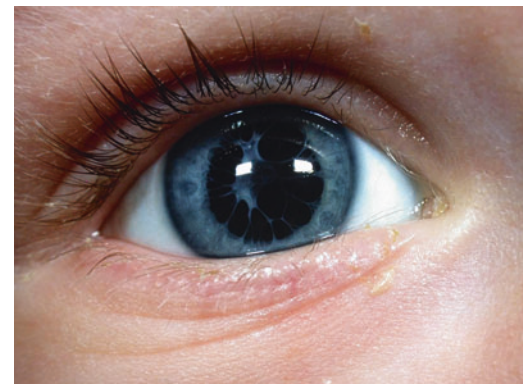
Definition

The presentation of incomplete involution of the in utero pupillary membrane with or without accompanying blood vessels from the underlying tunica vasculosa lentis.

Structure

In utero, the neural crest-derived iris stroma extends across the fetal pupil with strands arising from the iris collarette. There may be communications with the underlying tunica vasculosa lentis, a network of vessels formed by the anterior extension of the hyaloid artery, on the anterior lens surface especially in the peripheral regions. In the third trimester, these strands that cross the pupil resorb. Regression is aided by macrophage phagocytosis, the dysfunction of which may predispose to pupillary membranes. If there is failure of resorption, a pupillary membrane (Fig. 1) may be seen postnatally.

Persistent pupillary membranes (PPM) are usually spontaneous, random occurrences. There are rare reports of autosomal dominant inheritance and documented correlation with TORCH infections. Although most often isolated, these membranes may be seen in association with other anterior segment defects such as microcornea, microphthalmos, coloboma, and megalocornea.



Persistent Pupillary Membrane, Fig. 1 Photograph of a persistent pupillary membrane (Courtesy of Dr. Alex V. Levin, Wills Eye Institute)

Function

None

Clinical Relevance

Presentation

PPM are present in 95% of newborns and 20% of adults; the decrease in incidence with advancing age is felt to be due to natural dissolution perhaps induced by the daily movements of the pupil. Persistent pupillary membranes have variable presentations. Most often they are fine gray, filamentary projections extending from the iris collarette; the ends may be free floating in the anterior chamber or attached to another area of the iris collarette. Origination from the collarette distinguishes persistent pupillary membranes from inflammatory membranes that arise from the borders of the pupil. Pupillary membranes may appear pigmented. Rarely, they may be thick and hyperplastic, obstruct the visual axis, or be associated with attachment to the anterior lens capsule and predispose to localized anterior polar cataract.

Differential Diagnosis

- Inflammatory membrane/posterior synechiae
- Microcoria
- Axenfeld-Rieger syndrome

Significance

Even when substantial in size, PPM are rarely clinically significant. Associated anterior lens opacities are usually not in the visual axis, and cataracts seldom progress. Rarely, membranes may bleed if traumatized. In premature infants, cases have been reported in which a vascular connection between the pupillary membrane and the tunica vasculosa lentis acted as a conduit for the spread of organisms (e.g., *candida*) causing lens abscess in a septic child. Finally, if particularly large, PPM may obstruct the visual axis and cause amblyopia. Some authors classify these as separate entities called hyperplastic persistent pupillary membranes.

Treatment

Most PPM are small and either resolve or become asymptomatic by 1 year of age. If visually significant, medical therapy with pupillary dilation, without paralysis of accommodation (e.g., phenylephrine 2.5%), is usually effective. Rarely, laser therapy to the strands or surgical management, including iridectomy or pupilloplasty, have been performed to improve visual prognosis. After surgery, careful monitoring for the development of cataract, amblyopia, and glaucoma is necessary.

Cross-References

- ▶ Axenfeld-Rieger Syndrome; Mesodermal Dysgenesis; Leukomas
- ▶ Megalocornea
- ▶ Microcornea
- ▶ Microphthalmos
- ▶ Pigment Epithelium, Ciliary Body, and Iris

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Persistent Tunica Vasculosa Lentis

- ▶ Persistent Hyperplastic Primary Vitreous

Petrous Apicitis

- ▶ Gradenigo Syndrome

PEX

▶ Pseudoexfoliation Syndrome

Phacoemulsification and Posterior Chamber Intraocular Lens (IOL) Implantation

▶ Phacotrabeculectomy
▶ Phacoviscocanalostomy

Phacofragmentation

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Synonyms

Manual phacofragmentation

Definition

Phacofragmentation is a surgical technique for lens removal and is used in refractive and cataract surgery. This technique means the manual deterioration of the crystalline lens nucleus and the removal of lens pieces through a 4–5 mm wound.

Epidemiology

Cataract surgery is the most common surgery worldwide. Detailed data about the incidence of cataract surgery do not exist, but there are approximately ten million operations per year worldwide. The frequency and the operation technique varied among developed and undeveloped countries. In the USA nearly 80% of all cataract surgeries are accomplished by phacoemulsification. Phacofragmentation is an operation method that is accomplished in special cases when the nucleus of the crystalline lens is probably very hard and phacoemulsification might be problematic.

History

Extracapsular cataract extraction was performed since the middle of the eighteenth century. In former times the extraction of the nucleus happened as a mass without fragmentation through a wide incision.

Large incisions have several disadvantages such as problems with wound healing, vitreous loss, or infections. In 1988 Kansas et al. published in addition to the small incision technique of phacoemulsification another small incision cataract extraction technique using manual phacofragmentation. Since that time the operation method of phacofragmentation underwent several changes and amendments.

Clinical Features

The utilization of phacofragmentation is reserved for difficult cases in cataract surgery. In cases of advanced cataract, the preferred operation method of phacoemulsification is not suitable because of the callous nucleus of the lens. In these cases phacoemulsification can affect higher complications because of the higher ultrasound energy for deterioration of the hardened nucleus such as endothelial decompensation. Another reason for practicing phacofragmentation is a luxated lens in the vitreous body because of ocular trauma or connective tissue diseases such as Marfan's syndrome, homocystinuria, or Marcheani's syndrome. Lens removal is then advocated because it may induce uveitis and glaucoma. In these cases

phacofragmentation is often combined with pars plana vitrectomy.

Test

To examine best postoperative results thorough slit-lamp examination with dilated pupil, Scheimpflug imaging and measurement of uncorrected and best spectacle-corrected visual acuity are essential.

Etiology

See "Clinical Features" section above.

Treatment

Several different methods of phacofragmentation have been employed such as quarters extraction technique or prechop manual phacofragmentation.

The prechop manual phacofragmentation is described here. The nucleus in this technique is manually split into two fragments by prechopper forceps and the fragments removed through a 5.5–6.5 mm temporal clear corneal incision. After capsulorhexis, hydrodissection, hydrodelineation, and surface cortex aspiration, a prechopper forceps is gently passed into the center of the nucleus core and the nucleus is fragmented into two pieces. Each piece is prolapsed into the anterior chamber and extracted with corneal forceps and hooks via small incision.

Cross-References

- ▶ Clear Corneal Incision
- ▶ Pars Plana Vitrectomy
- ▶ Phacoemulsification and Posterior Chamber Intraocular Lens (IOL) Implantation
- ▶ Secondary Glaucoma in Uveitis

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Phacomorphic Angle-Closure Glaucoma

▶ Lens Dislocation

Phacotrabeculectomy

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Synonyms

Combined trabeculectomy; Phacoemulsification and posterior chamber intraocular lens (IOL) implantation

Definition

A surgical technique that is used in patients with a coexisting affection of glaucoma and cataract. The technique includes a combination of phacoemulsification, intraocular lens

implantation, and trabeculectomy. Phacoemulsification and intraocular lens implantation are surgical treatments for cataract, and trabeculectomy is a penetrating filtering surgical procedure for various types of open-angle and normal-tension glaucoma. The technique of phacotrabeculectomy can include either both operations performed through the same incision (a one-site procedure) or through separate incisions (two-site procedure).

Epidemiology

Combined glaucoma and cataract surgeries are increasing in popularity because both cataract and glaucoma are age-related diseases, and the recent technical improvements in small-incision phacoemulsification have reduced the risk of postoperative or tissue trauma.

History

Lyle et al. first introduced the term phacotrabeculectomy in the literature in 1991. The combined procedure of phacoemulsification, posterior chamber intraocular lens (IOL) implantation, and trabeculectomy has been advocated for treating coexisting glaucoma and cataract. In several studies since the early 1990s, a positive effect of phacotrabeculectomy on the reduction of eye pressure was shown. Negative side effects were also seen as there are bleb leaks, hypotony, flat anterior chamber, choroidal detachment, and endophthalmitis. That was a reason for the development of other combined surgical techniques for the reduction of the eye pressure at the end of the 1990s as there was phacoviscoanalostomy.

Clinical Features

According to the World Health Organization, cataract is the first and glaucoma is the third most common cause of blindness worldwide. A major risk factor for both of these diseases is aging, and therefore the coexistence of cataract and glaucoma is not uncommon.

A combined cataract and glaucoma surgery is an appealing therapeutic approach because of the increased risk of cataract development in some glaucoma patients, the increased risk of cataract development after glaucoma surgery, and the need to minimize trauma and cost induced by two surgical procedures.

Test

For checking the postoperative outcome, it is necessary to control the intraocular pressure in close meshed gaps. Furthermore uncorrected and best-corrected vision acuity and thorough slit-lamp examination are essential constituent parts of postoperative control.

Another surgical procedure for combined treatment of cataract and glaucoma is:

- Phacoviscoanalostomy

Cross-References

- ▶ Cataract, Causes and Treatment
- ▶ Combined Trabeculectomy
- ▶ Phacoemulsification and Posterior Chamber Intraocular Lens (IOL) Implantation

Further Reading

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Phacoviscocanalostomy

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Synonyms

Combined viscocanalostomy; Phacoemulsification and posterior chamber intraocular lens (IOL) implantation

Definition

A surgical technique that is used in patients with a coexisting affection of glaucoma and cataract. The technique includes a combination of phacoemulsification, intraocular lens implantation, and viscocanalostomy. Phacoemulsification and intraocular lens implantation are surgical treatments for cataract, and viscocanalostomy is a non-penetrating filtering surgical procedure for various types of open-angle and normal-tension glaucoma.

History

Viscocanalostomy is a relatively new, surgical procedure that was first described and developed by Stegmann et al. in 1999. Then phacotrabeculectomy and trabeculectomy were common surgical procedures for reducing the eye pressure in patients with glaucoma. These techniques are known to be connected with several potentially serious complications as there are bleb leaks, hypotony, flat anterior chamber, choroidal detachment, and endophthalmitis. In contradiction viscocanalostomy in combination with phacoemulsification is reported to efficiently and safely reduce intraocular pressure (IOP) while improving visual acuity.

Epidemiology

Combined glaucoma and cataract surgeries are increasing in popularity because both cataract and glaucoma are age-related diseases, and the recent technical improvements in small-incision phacoemulsification have reduced the risk of postoperative or tissue trauma.

Clinical Feature

According to the World Health Organization, cataract is the first and glaucoma is the third most common cause of blindness worldwide. A major risk factor for both of these diseases is aging, and therefore the coexistence of cataract and glaucoma is not uncommon.

A combined cataract and glaucoma surgery is an appealing therapeutic approach because of the increased risk of cataract development in some glaucoma patients, the increased risk of cataract development after glaucoma surgery, and the need to minimize trauma and cost induced by two surgical procedures.

Test

For checking the postoperative outcome, it is necessary to control the intraocular pressure in close meshed gaps. Furthermore uncorrected and best-corrected vision acuity and thorough slit-lamp examination are essential constituent parts of postoperative control.

Differential Diagnosis

Another surgical procedure for combined treatment of cataract and glaucoma is:

– Phacotrabeculectomy

Description

Viscocanalostomy can be both first and second step of the procedure. The original idea of

phacoviscocanalastomy was an aqueous humor passage from the anterior chamber through an intact window in Descemet's membrane above Schwalbe's line into a subscleral lake and ultimately through surgically made openings into Schlemm's canal.

Cross-References

- ▶ Cataract, Causes and Treatment
- ▶ Phacoemulsification and Posterior Chamber Intraocular Lens (IOL) Implantation
- ▶ Phacotrabeculectomy

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Phakic Intraocular Lens

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Synonyms

Phakic IOL; PIOL

Definition

An additional artificial intraocular lens to correct a refractive error that is placed in an eye in which the existing crystalline lens has not been removed (Kohnen and Koch 2006).

Epidemiology

Phakic IOLs are implanted throughout the world with rising numbers. Due to its spectrum of indications, phakic IOL surgery accounts for less than 1–2% of all refractive surgical procedures.

History

The first experience with phakic IOLs was by Barraquer and Strampelli in the middle of the last century using an anterior chamber design. Due to the high complication rate that often demanded explantation of the IOL, this novel method was abandoned and no phakic IOL was manufactured or implanted for the following 20 years. In the 1970s, J. Worst developed an iris-fixated anterior chamber IOL, which was first implanted into aphakic eyes by P. Fechner (Fechner and Alpor 1986). Several modifications of this IOL have been performed since then in order to gain more space between the phakic IOL and the cornea in order to increase safety for the corneal endothelium. In the 1980s and the 1990s, great technological progress in both IOL manufacturing and surgical techniques was attempted, and several polymethyl methacrylate (PMMA) angle-supported anterior chamber phakic IOLs were developed (Hardten et al. 2003). However, all of them were subsequently phased out of the market due to unacceptable rates of complications, including corneal endothelial cells loss, pupil ovalization, glare and halos, and chronic anterior uveitis. Current studies with the newly developed foldable anterior chamber angle AcrySof show that these problems can be reduced and that safety of the corneal endothelium is ensured.

Clinical Features

Implantation of phakic IOLs has been demonstrated as an effective, safe, predictable, and stable procedure to correct moderate and high refractive errors. Complications are rare and are mostly related to the site of implantation. However, longer follow-up studies are needed to establish long-term safety of these lenses. Development of new anterior segment imaging devices is changing preoperative and postoperative management of phakic IOLs, increasing safety profiles and allowing for a more accurate follow-up. Moreover, exact measurements of anterior chamber diameter, anterior chamber depth, and ciliary sulcus diameter are improving the phakic IOL selection and thus decreasing the risk of unwanted complications. The potential clinical applications and the range of information they may yield are being continuously explored and further developed.

Tests

In order to ensure safety of phakic IOLs, several inclusion criteria must be considered:

- Age over 21 years
- Stable refraction of at least 1 year
- Absolute contraindication for corneal surgery
- Iridocorneal anterior chamber angle of at least 30°
- Corneal endothelial cell count over 2,300/mm^2 (2,500 >21 years, 2,000 >40 years)
- Anterior chamber depth of at least 2.7 mm for Acrysof and Artisan-Verisyse
  For implantable collamer lens (ICL), at least 2.8 mm for myopic and at least 3 mm for hyperopic lenses
  For phakic refractive lens (PRL), at least 2.5 mm
- Regular pupillary function
- Mesopic pupillary diameter below 5–6 mm

Differential Diagnosis

An aphakic IOL is an IOL that is implanted in an aphakic eye and is usually placed in the capsular bag. A supplementary pseudophakic IOL is an IOL that is implanted in an eye with an artificial IOL (see also piggyback or Add-On IOL).

Etiology

Phakic IOLs are divided into anterior chamber phakic IOLs, iris-fixated phakic IOLs, and posterior chamber phakic IOLs.

Treatment

Implantation of a phakic IOL is usually a treatment option for eyes that cannot undergo excimer laser correction, e.g., due to higher ametropia (over minus 8 D or over plus 4 D) or underlying corneal keratectatic disease.

Cross-References

- ▶ Anterior Chamber
- ▶ Artisan Lens
- ▶ Foldable Intraocular Lens
- ▶ Implantable Collamer Lens
- ▶ Intraocular Lens
- ▶ Iris-Fixated Phakic Intraocular Lens
- ▶ Phakic Refractive Lens
- ▶ Piggyback Intraocular Lens
- ▶ Posterior Chamber Phakic Intraocular Lens
- ▶ Verisyse Iris-Supported Phakic Intraocular Lens

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Phakic IOL

- ▶ Phakic Intraocular Lens

Phakic Refractive Lens

► PRL Phakic Intraocular Lens

Pharmacologic Anisocoria

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Definition

Pharmacologic anisocoria refers to anisocoria as caused by a pharmacological agent. Anisocoria further defines a state of unequal pupillary size between the two eyes (typically greater than 0.4 mm in diameter).

Etiology

Pharmacologic anisocoria specifically refers to anisocoria due to the iris sphincter or dilator muscle by a pharmacological agent.

Mydriatic agents include sympathomimetic and parasympatholytic medications. The sympathomimetics include α1-adrenergic agonists (e.g., epinephrine or neosynephrine containing eye or nasal drops or sprays, the topical glaucoma agent, apraclonidine, and various cardiac medications). These medications act to directly stimulate the iris dilator muscle by increasing norepinephrine activity on α1 receptors. Other mydriatic agents include recreational, psychoactive drugs such as cocaine (inhibits reuptake of norepinephrine) and amphetamine (stimulates release of norepinephrine). These same indirect sympathomimetic agents can be used topically to pharmacologically test the integrity of the ocular sympathetic pathway.

Mydriatic agents whose mechanism involves blocking the iris sphincter muscle in order to decrease parasympathetic tone (i.e., parasympatholytics) include anticholinergic medication. Common anticholinergic medication involved in pharmacologic anisocoria includes diagnostic eye drops used for dilated fundus exams (e.g., tropicamide) and therapeutic eye drops (e.g., atropine, cyclopentolate) including some over the counter parasympatholytic topical preparations. Ipratropium inhalers, scopolamine transdermal patches, and rarely chronic use of sinus decongestants like diphenhydramine are additional anticholinergic agents responsible for anisocoria. Further, exposure to jimsonweed and other belladonna alkaloids from the *Datura* genus may induce unilateral mydriasis.

Pharmacologic anisocoria may also be a result of miotic agents which cause constriction of the pupil in comparison with the other pupil. Chronic use of topical pilocarpine and other muscarinic agonists in glaucoma therapy permanently affects the pupil's ability to dilate through direct stimulation of M3 receptors on the iris sphincter muscle. Exposure to acetylcholinesterase inhibitors used in insecticides and flea collars can also produce pharmacologic miosis or anisocoria.

Clinical Presentation

Pharmacologic anisocoria in contrast to physiologic anisocoria is typically greater than 0.4 mm. The anisocoria may be greater in the dark (failure

to dilate) or in the light (failure to constrict). Conjunctival blanching and eyelid retraction may occur in cases caused by sympathomimetic drugs. Assessment of accompanied symptoms is critical in order to further establish the etiology of anisocoria and rule out more serious pathologies.

Diagnostics

Performing a thorough patient history relating to medication history, recreational drug use, and environmental exposure is key in diagnosing pharmacologic anisocoria. Physical examination of the pupils should be performed in dark and bright light to first determine which pupil is abnormal. When conducting the pupillary light reflex examination in bright light, if the larger pupil constricts poorly, the anisocoria will typically involve a mydriatic pupil. If the smaller pupil does not effectively dilate in dim light, then the abnormal pupil is miotic. Pharmacologic mydriasis due to a parasympatholytic agent produces anisocoria that is worse in the light.

Further diagnostic methods for pharmacologic anisocoria caused by mydriatic agents include pilocarpine testing. The direct-acting parasympathetic agent pilocarpine 1% can be used to determine if there is pharmacologic blockade. Note that pilocarpine testing is not as useful for sympathomimetic-related mydriasis and topical pilocarpine is usually a stronger stimulus for the sphincter to constrict than the adrenergic stimulation of the iris dilator muscle.

Finally, appropriate laboratory testing via serum or urine testing for verification of suspected systemic organophosphate exposure and drug overdose.

Differential Diagnosis

Physiologic anisocoria, Horner's syndrome, Adie's tonic pupil, oculomotor nerve palsy, eye trauma resulting in mechanical damage of the iris, uveitis, neovascularization of the iris in diabetic eye, or ocular ischemic syndrome.

Prophylaxis

Avoid use of offending pharmacological agents.

Therapy

Discontinuation of responsible pharmacological agent if possible.

Prognosis

Pharmacologic anisocoria should resolve over days or weeks depending upon the pharmacokinetics of the responsible agent.

Epidemiology

Pharmacologic anisocoria from inadvertent exposure typically occurs in health care workers with access to topical agents but may occur in any age, either gender, and any ethnic group. Patients with blue irides may have more noticeable effects of pharmacologic anisocoria due to differential drug absorption after exposure.

P

Cross-References

- ▶ Anisocoria
- ▶ Pupillary Light Reflex

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Phenothiazine Retinopathy

- ▶ Chlorpromazine, Retinal Degeneration

Phlycten

▶ Phlyctenules

Phlyctenular Keratoconjunctivitis

▶ Phlyctenules

Phlyctenules

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Synonyms

Phlycten; Phlyctenular keratoconjunctivitis; Phlyctenulosis

Definition

A phlyctenule is an inflammatory nodule of the ocular surface, found in the cornea or the conjunctiva. It is often located near the limbus but can occur anywhere in the cornea or conjunctiva. Clinically, the lesions are nodular, are yellow or pink white in color, and are associated with surrounding neovascularization in the cornea or adjacent hyperemia of the bulbar conjunctiva. They can become ulcerated. The word "phlyctenule" originates from the Greek word "phlyktaina," meaning "blister." Phlyctenulosis is believed to be a type IV hypersensitivity to bacterial antigens, most notably *Staphylococcus* species, *Propionibacterium acnes*, and other bacterial antigens. In addition to its association with systemic *Mycobacterium tuberculosis* infection, phlyctenulosis has also been associated with systemic worms and parasites. The meibum of patients with phlyctenular keratoconjunctivitis has been reported to contain bacteria such as *Staphylococcus epidermidis* and *Corynebacterium* species. Phlyctenulosis affects mostly children and young adults and has been associated with eyelid margin disease. Histologically, monocytes and monocyte-derived cells predominate. Polymorphonuclear leukocytes, T lymphocytes, and – to a lesser extent – B lymphocytes and plasma cells can be found as well. The mainstays of treatment are eyelid hygiene and oral antibiotics, particularly when the phlyctenule is associated with blepharitis related to *Staphylococcus* or rosacea. Topical steroids are also used to reduce inflammation and neovascularization. Sometimes, the lesion can be refractory to topical steroids. In such cases, topical cyclosporin A or tacrolimus can be offered as treatment.

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Phlyctenulosis

▶ Phlyctenules

Phosphene

▶ Electrically Evoked Potentials

Photic Damage

▶ Light Toxicity, Free Radical Damage; Photic Damage/Phototoxicity, Free Radical Damage

Photochromic Foldable Intraocular Lens

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Definition

The term "photochrome" means capable of darkening or changing color when exposed to light. Photochromism can be defined as the ability of a material to reversibly change its visible absorption spectrum on exposure to activating radiation and to revert to its original absorption spectrum on removal of the activating radiation or on substituting radiation of a different wavelength (Werner et al. 2006).

Epidemiology

One of the most famous reversible photochromic applications is color changing lenses for sunglasses, as found in eyeglasses.

History

Organic photochromic compounds have been known for over a hundred years and date back to the era of Alexander the Great. However, they excited little commercial interest until the 1950s. Inspired by the work of E. Fischer and Y. Hirshberg who first reported photochromism in spiropyran analogues in 1952, intense studies on photochromic compounds have continued up to the present. In ophthalmology, yellow IOLs were introduced on the market in the 1990s with the idea that light with a short wavelength may damage the retinal pigment epithelium and the neurosensory retina (Kohnen and Koch 2009). Medennium Inc. recently developed an IOL with photochromic properties. According to the manufacturer, this IOL has an ultraviolet (UV) near-blue absorption curve similar when exposed to UV light, while it behaves as a standard UV-absorbing IOL in an indoor environment.

Clinical Features

The clinical benefit of photochromic IOLs is currently under investigation.

Tests

The clinical benefit of photochromic IOLs is currently under investigation.

Differential Diagnosis

Blue-filter IOLs might inhibit the phototoxic effect of blue light on the macula and therefore reduce the risk of developing age-related macular degeneration. Yellow IOLs might decrease contrast sensitivity and color vision under mesopic conditions (Wenzl et al. 2009). Photochromic IOLs are clear under mesopic and scotopic conditions and turn yellow under photopic conditions.

Etiology

The term photochromic refers to greek "phos" = light and "chroma" = color.

Treatment

See also entry "▶ Cataract Surgery" and "▶ Intraocular Lens."

Cross-References

- ▶ Acrylic Intraocular Lens
- ▶ Cataract Surgery
- ▶ Foldable Intraocular Lens
- ▶ Hydrophilic Acrylic Intraocular Lens
- ▶ Hydrophobic Acrylic Intraocular Lens
- ▶ Intraocular Lens
- ▶ Silicone Intraocular Lens

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Photocoagulation

- ▶ Laser Focal Treatment

Photodisruption

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Introduction

Photodisruption is the disruption of tissues due to the rapid ionization of molecules caused by exposure to laser light. It is a commonly used technique for performing minimally invasive intraocular surgery. The first clinical use of photodisruption was demonstrated in 1972, when photodisruption with a pulsed ruby laser was used to treat open-angle glaucoma. However, it was not until the development of Q-switched Nd:YAG lasers in the early 1980s that photodisruption became truly clinically useful.

Mechanism of Action

Biological tissue is not a very strong absorber of visible light; however, a tightly focused pulsed laser can produce very high intensity of light in the focal volume and result in the nonlinear absorption of the light. This absorption of energy causes the temperature in the focal volume to rise to ~10,000 K, resulting in the formation of plasma (via thermionic emission of electrons) which then expands through avalanche or cascade ionization. The rapid temperature increase in the plasma is accompanied by a pressure increase in the focal region. This increased pressure and plasma expansion cause the generation of a shockwave and the formation of a cavitation bubble, which eventually collapses.

The plasma formation is the main mechanism that mediates the surgical effect of photodisruption, as it essentially causes evaporation of material from the focal volume of the laser beam, allowing the high-precision cutting of tissue. Since the entire process is mediated by nonlinear effects, only a very small focal volume is affected. No thermal side effects from the laser light are observed and very little damage of the surrounding tissue is expected. However, the generation of the shock wave and cavitation bubble can cause disruption of peripheral tissue around the focal volume. This additional disruption may sometimes be desirable, but at other times contributes toward unwanted side effects of the surgical procedure.

Applications

The high-precision cutting and relatively low peripheral damage of the photodisruption technique make it ideally suited for micromachining applications and minimally invasive surgery. Of the two, the clinical application of disruption is

more widespread. In fact, photodisruption is now a well-established technique for performing intraocular surgery: iridotomy for acute angle-closure glaucoma and capsulotomy for secondary cataract are routinely performed using this technique, and other procedures such as pupillary membranectomy, synechialysis, and division of the vitreous membranes have also been performed successfully. Typically used systems for clinical photodisruption involve Nd:YAG lasers with pulse widths of a few nanoseconds and energies in the range of low millijoules.

The major advantage of photodisruption is that it is a minimally invasive technique, requiring no surgical entry into the eye and can be easily performed as an outpatient procedure. The major disadvantage is the potential damage to the tissue surrounding the laser focus. One way to circumvent the damage to peripheral tissue is to use laser pulses with lower energy. Picosecond or femtosecond laser pulses, which have a lower energy threshold for plasma formation than nanosecond pulses, have been shown to improve the precision and minimize unwanted disruption in Nd:YAG ocular surgery. In fact, it is possible to photodisrupt tissues with subcellular precision using femtosecond pulses. Thus it may be possible to extend the use of photodisruption to applications requiring single-micron-level precision.

Cross-References

- ▶ Capsulotomy
- ▶ Iridotomy
- ▶ Open-Angle Glaucomas
- ▶ Striate Keratopathy, Intraocular Surgery Causing

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Photokeratoscopy

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Synonyms

Corneal topography; Placido disk; Placido ring

Definition

Calculation of the corneal power based upon the manner in which light is reflected from the anterior surface of the cornea.

Purpose

Determination of corneal power.

Principle

Rings of light are reflected from the anterior surface of the cornea producing an image which is captured by a computerized keratometer. The pattern of the reflection is analyzed to determine the anterior corneal curvature. This curvature is then converted into corneal power.

The main assumption in this mode of keratometry is that the posterior corneal curvature is assumed to be normal. The anterior surface of the cornea is converging (positive), whereas the posterior surface is diverging (negative). These keratometers combine a measured anterior corneal curvature and an assumed posterior curvature

to provide an estimated total corneal power based upon Snell's law of refraction. To compensate for the assumed posterior curvature, a decreased index of refraction is used for corneal power calculations: the cornea has an actual index of refraction of 1.376, whereas most photokeratoscopes use an index of refraction of 1.3375 (Budak et al. 1999).

Photokeratometers provide information on axial power (the power relative to the visual axis) and instantaneous power (the power relative to the points immediately around a corneal location). Axial power maps offer a more global description of shape, while instantaneous radius of curvature maps provides the details of local curvature (Gobbi et al. 1998). Astigmatism is calculated based upon the steepest (highest power) and flattest (lowest power) meridians at various distances from the optical axis. The symmetry or irregularity of this astigmatism along with the location of maximum corneal power is useful for the diagnosis of corneal ectatic diseases (Piñero et al. 2010).

Indication

Need for determination of corneal power/astigmatism.

Clinical concern for corneal topography irregularity (i.e., keratoconus, keratoglobus, pellucid marginal degeneration, irregular astigmatism, etc.).

Advantage/Disadvantage

This exam is noninvasive and rapid and yields valuable information related to corneal power, astigmatism, and corneal abnormalities related to changes in corneal shape such as keratoconus, pellucid marginal degeneration, and keratoglobus. (See figures for examples of keratoconus and regular astigmatism.)

The main limitation for this exam is its assumption of normal posterior corneal topography. It is known that the posterior curvature of the cornea can help in the early diagnosis of keratoconus and contributes to corneal astigmatism. Devices that map the posterior cornea may be of use in providing a more complete and accurate power of the cornea and assist in the diagnosis of ectatic disease (Tang et al. 2005).

There are two main types of imaging for the posterior cornea. The first method uses placido technology to determine the anterior corneal curvature and reconstructs the posterior corneal curvature using pachymetry determined by either scanning slit technology (used by the Orbscan II) or by Scheimflug imaging (used by the Pentacam, Sirius, and Galilei). The second method involves directly imaging the anterior and posterior cornea using an anterior segment optical coherence tomography (ASOCT) unit and reconstructing pachymetry from this data. More information on this can be found in the "Computerized Corneal Topography" section.

Cross-References

- ▶ Computerized Corneal Topography
- ▶ Ectasia, Corneal
- ▶ Pellucid Marginal Degeneration

References

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Photometric Contrast Sensitivity

► Contrast Sensitivity

Photomicroscopy, Specular

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Synonyms

Corneal endothelium image; Specular photomicroscopy

Definition

Specular microscopy (contact and noncontact techniques), a camera-mounted, slit-lamp-like instrument, allows visualization and photography of the corneal endothelial mosaic. Wide-field microscopy encompasses 200 cells per frame and can be done at multiple corneal sites, usually centrally. At birth the endothelial density is about 6,000 cells, and in adult the normal endothelial density averages 2,400 cells per mm^2 (1,500–3,500 range) and decreases with age. The normal endothelial cell is shaped as a regular hexagon.

There are several specular microscopy instruments commercially available, both contact and noncontact. All the instruments have computer integration and semi- or fully automated analyses. Some instruments allow manual analysis and/or adjustments to the automated system. Perhaps, the most widely used clinical instrument in the United States is the *Konan NonCon Robo* series. In addition, HAL offers a contact specular microscope. Although it is less comfortable for the patient, it provides sharp, wide-field images regardless of corneal thickness or disease.

Purpose

Specular microscopy is the study of the changes in different layers of the cornea under very high magnification (100 times greater than slit-lamp biomicroscopy), which is mainly being used to assess the endothelial layer. The image is analyzed with respect to the cellular size, shape, density, and distribution.

Principle

When a light beam of the specular photomicroscope passes through the cornea, it encounters a series of interfaces between optically distinct regions. Small amount of light is reflected specularly (i.e., like a mirror) back toward the photomicroscope when the angle of reflection is the same angle of incidence. This specular light is captured by the photomicroscope and forms an image which can be photographed and analyzed. The following parameters can be calculated from specular images:

- Cell density: the normal endothelial cell density decreases with age. Endothelial cell normally exceeds 3,500 cells/mm^2 in children and gradually declines with age to approximately reach 2,000 cells/mm^2 in older people. An average cell density's value for adults is 2,400 cells/mm^2 (1,500–3,500), with cell size's mean of 150–350 μm^2.
- Coefficient of variation: the standard deviation of the mean of cell area divided by the mean cell area gives the coefficient of variation. It is a unit-less number, normally less than 0.30. Polymegathism is an increased variation in individual cell area. It is typically increases with wearing contact lens. Corneas with significant polymegathism (more than 0.40) might not tolerate intraocular surgery.
- Percentage of hexagonal cell: the percentage of cells with six apices should ideally approach about 100% and decrease with age; however, lower percentage of cells indicates a diminishing state of health of the endothelium. Pleomorphism is increased variability in cell

shape. A cornea with high pleomorphism (more than 50% non-hexagonal) might not tolerate intraocular surgery.

Indication

- Prior to surgery, evaluating the functional reserve of the corneal endothelium prior to intraocular surgery is the most important indication. A clear cornea with normal pachymetry (i.e., thickness) is not necessarily associated with normal endothelial morphology or cell density.
- Donor cornea: evaluation regarding suitability for penetrating keratoplasty.
- To demonstrate pathology: particularly cornea guttae irregularities and posterior polymorphous dystrophy.

Contraindication

While specular microscopy is desirable for evaluation of wide assortment of corneal diseases, direct applanation of the objective (contact) may be contraindication in patients with irregular corneal epithelium and/or epithelial dystrophy or patients wearing therapeutic or continuous-wear hydrogel lenses that should not be removed.

In general optimal photographs are obtained when the cornea is relatively thin and clear with minimal scarring or edema.

Advantage/Disadvantage

The advantages of the microscopy are that it can detect pleomorphism (cells deviating from normal shape), cell dropout as in Fuchs dystrophy, and polymegethism (abnormal cell size variation). Which all contribute to endothelial dysfunction and corneal edema.

The microscopy has several disadvantages. The corneal epithelial cells do not normally present a flat surface suitable for specular microscopy. Also, most specular microscopic studies of the corneal endothelium determine mainly the endothelial cell density of the central endothelium in order to attempt to consistently examine the same endothelial cell area over time. In addition, changes in the central corneal endothelium in both density and morphology may take some time (months or years) to be reflected. The specular microscopy does not reflect the impact of a surgical procedure that primarily damages the peripheral cornea. Moreover, the paracentral and the peripheral endothelium, in particular superiorly, have higher cell density and may assist in maintaining central endothelial density and function.

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Photophobia

► Day Blindness (Hemeralopia), in Cone Dystrophies

Photoreceptor Cells

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Definition

Light-sensitive cells residing in the posterior layer of the neural retina.

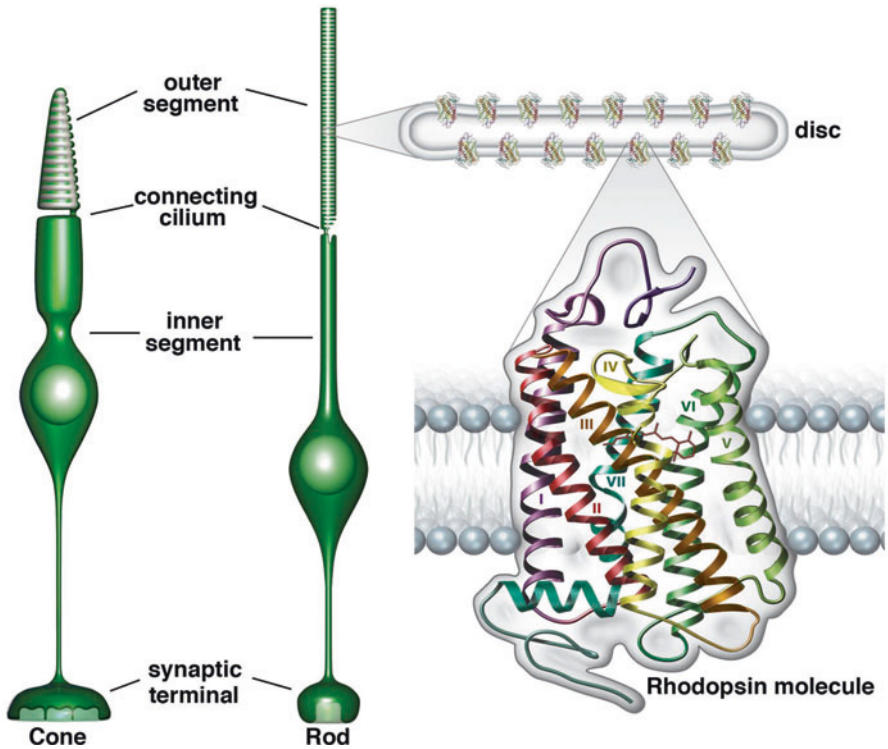
Basic Characteristics

Structural Specialization

The two basic types of photoreceptor in the human retina are rods and cones. Rods outnumber cones by nearly 20:1. In general, photoreceptors consist of an outer segment, an inner segment, and a synaptic terminal (see Fig. 1). The inner segment is the metabolic center of the photoreceptor, housing the nucleus, mitochondria, and other cellular machinery. The outer segment contains the proteins involved in phototransduction. Connecting the inner and outer segments is the connecting cilium, a microtubule-based structure, through which all newly synthesized proteins are transported to the outer segment. The outer segment of both rods and cones consists of stacks of membranous disks – in cones the disks are continuous with the plasma membrane of the cell, whereas in rods they are free-floating. The photopigments are integral membrane proteins located within the lipid membrane of these outer segment disks (see Fig. 1). Photopigment is very abundant with some 100 million photopigment molecules being embedded throughout the outer segment of each rod and cone cell. It is estimated that photopigments represent about 90% of the protein molecules in the outer segment.

Functional Specialization

While both are involved in the detection of light, rods and cones provide distinct functional utility for the human visual system. This enables the visual system to function over a wide range of light intensities. Rods are much more sensitive than cones and thus function well at low light levels (rods can detect a single photon of light!). Cones function at higher light levels and are less sensitive. Paradoxically, the majority of our vision is cone based, despite the fact that cones are outnumbered by rods in the human retina. Another important difference between rods and cones is that cones do not saturate, whereas rods do. Saturation means that as the light level is



Photoreceptor Cells, Fig. 1 Basic structure of rod and cone photoreceptors (Reprinted with permission from Elsevier)

gradually increased, there reaches a point where rods will no longer increase their response in proportion to the stimulus intensity. A final difference between rods and cones is their spectral response properties. This feature is determined by the photopigment present in the outer segment – rods contain a photopigment with maximum sensitivity at 500 nm. A given cone photoreceptor will contain one of the three spectral subtypes of cone photopigment, short-, middle-, or long-wavelength sensitive (S, M, and L), which have peak sensitivity at 415, 530, and 560 nm, respectively.

Topographical Arrangement of Rods and Cones

The rods and cones are distributed unevenly across the human retina. The central fovea contains exclusively cones, the first rods don't appear until about 175 μm from the foveola. Rod density peaks around 12° eccentricity to a value of 180,000 rods/mm^2. Despite changes in density, rods remain nearly constant in diameter across the retinal surface (about 2 μm). Peak cone density occurs in the fovea, and there is significant intersubject variation in peak cone density, from 80,000 to 300,000 cones/mm^2. Cone density falls off precipitously moving away from the fovea in all directions, dropping to about 30,000 cones/mm^2 at 1.5° eccentricity. As cone density falls, the average cone diameter increases. After about 10°, the density of cones reaches a near constant value of 7,000 cones/mm^2, until the extreme edge of the neural retina, where there is an increase in the density of cones to about 15,000 cones/mm^2.

As stated earlier, there are three spectral subtypes of cone – S, M, and L. S cones comprise less than 10% of the total cone number and can be distinguished from L and M cones based on their more cylindrical shape and that they connect to distinct neural circuitry. Like the rod and cone mosaics as a whole, the S-cone distribution varies topographically. The density of S cones is lowest in the central fovea, with an S-cone-free zone of about 125 μm. Peak S-cone density occurs at about 1° eccentricity. There is a high degree of similarity between the L and M cones (perhaps the *only* difference between an L and an M cone is the respective photopigment). The L and M cone submosaics appear to be randomly interleaved, and L cones generally outnumber M cones in the human retina by a factor of 2, though there is inter- and intra-retina variation. For example, the relative ratio of L/M cones increases moving into the peripheral retina, and the central ratio can vary over a 40-fold range across individuals with normal color vision.

Cross-References

▶ Color Vision, Three Cone Opsins
▶ Retina, Structure of

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Photorefractive Keratectomy (PRK)

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Synonym

PRK

Definition

Photorefractive keratectomy (PRK) is a ▶ corneal refractive surgical treatment using the ▶ excimer laser for surface tissue ablation. It is known as the

first surgical technique to treat myopia with ► corneal excimer ablation. The first treatments were performed independently in the mid-1980s by Theo Seiler in Berlin and Marguerite McDonald in New Orleans. The surgical technique is rather simple: After scraping off the corneal epithelium, the excimer laser ablation is performed. Besides the advantages of simplicity and leaving a higher portion of corneal tissue unaltered than lamellar techniques, several disadvantages such as pain in the early postoperative period and a prolonged ► wound healing reaction including the formation of corneal haze and regression are described. These shortcomings led to the development of lamellar techniques such as LASIK on the one hand and to modifications such as LASEK (laser subepithelial keratomileusis) and epi-LASIK on the other hand. However, PRK and its modifications are still in use.

Cross-References

► Excimer Lasers
► Refractive Surgery

Phototherapeutic Keratectomy

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Synonyms

Excimer laser phototherapeutic keratectomy; PRK

Definition

Excimer laser procedure for treatment of superficial corneal diseases and surface irregularities by ablating superficial corneal tissue without damaging adjacent untreated tissue.

Epidemiology

As the number of corneal refractive surgery procedures is increasing, so will the number of PTK for treatment of complications.

History

After its introduction in 1983 to perform surface ablations of the cornea, the excimer laser was approved for PTK in 1988 by the Food and Drug Administration.

Clinical Features

The excimer laser emits high-energy ultraviolet radiation at a wavelength of 193 nm and enables the user to treat corneas at a very high precision rate.

Tests

Thorough slit-lamp examination of the eyes and keratometric, keratographic, and pachymetric readings are required for preoperative planning to assure the best possible results.

Differential Diagnosis

Other corneal treatment methods are:

- LASIK
- LASEK

Etiology

See History section above.

Treatment

After topical anesthesia, the epithelium is removed either with the laser or manually with a

blade. After the surface has been removed and Bowman's layer is exposed, the excimer laser is focused on the surface to remove the proper tissue. Finally the ablated surface is covered with a bandage contact lens and postoperative medication is given.

Cross-References

▶ Corneal Dystrophy
▶ PRK

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Phototoxic Maculopathy

▶ Arc Welding, Occupational Light Injury and

Phototoxicity

▶ Electromagnetic Energy/Radiation, Adverse Effects on Retina
▶ Light Toxicity, Free Radical Damage; Photic Damage/Phototoxicity, Free Radical Damage

Phototransduction Cone/Rod

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Definition

Biochemical cascade by which light energy is converted into electrical signals.

Basic Characteristics

Phototransduction occurs in the photosensitive cells of the human retina: photoreceptor cells (rods and cones) and the melanopsin-containing ganglion cells. As the photosensitive ganglion cells appear to employ phototransduction processes similar to invertebrates, we focus here on the phototransduction cascade of rods and cones.

Photopigment Structure

Human photopigments consist of a chromophore (11-*cis*-retinal) and a protein portion (opsin). The chromophore is covalently bound via a protonated Schiff base linkage with a lysine residue in the opsin molecule. The opsins are a member of the protein superfamily of G protein-coupled receptors (GPCRs). All GPCRs (including opsins) have seven transmembrane s domains, in addition to C-terminal, N-terminal, and short loops that reside outside the membrane (intra- or extracellular). It is the 11-*cis*-retinal that is light absorbing, though in solution its peak absorbance is at 380 nm. The linkage to opsin shifts the absorption spectrum into the visible region of the spectrum.

Phototransduction Cascade

Upon absorption of a photon, 11-*cis*-retinal undergoes an isomerization to all-*trans*-retinal. This occurs on the order of about 200 fs. This isomerization induces a conformational change in the opsin portion of the photopigment, which in turn leads to the activation of transducin. Transducin, in its inactive state, is bound to GDP. Upon activation, transducin releases GDP and binds GTP. The a-subunit of transducin (still bound to GTP) then dissociates from the band g-subunits. The a-subunit/GTP complex then activates phosphodiesterase, which catalyzes the breakdown of cGMP to 5′GMP. cGMP is needed to hold open the cGMP-gated (CNG) sodium channels, so the decreased concentration of cGMP causes the sodium channels to close. As a result, the photoreceptor cell hyperpolarizes and decreases its release of the neurotransmitter glutamate. The decrease in glutamate release causes a graded hyperpolarization of the OFF bipolar cells and a graded depolarization of the ON bipolar cells. The hyperpolarization of the

photoreceptor results in a closure of voltage-gated calcium channels, and the reduction in calcium concentration plays an important role in deactivation of the cascade (see below).

Deactivation of the Phototransduction Cascade

The reduction of calcium concentration enables guanylyl cyclase-activating protein (GCAP) to bind to guanylyl cyclase (GC), thus increasing its activity and converting GTP to cGMP. The decrease in calcium concentration also results in an increased affinity of the CNG channels for cGMP, due to the dissociation of calmodulin from the CNG channels. cGMP concentration rises, causing the reopening of the cGMP-gated sodium channels. In addition, the reduction in calcium causes recoverin (normally bound to calcium) to dissociate from rhodopsin kinase. The rhodopsin kinase phosphorylates the activated opsin molecule, which decreases its affinity for transducin. The final step of deactivation of opsin is the binding of arrestin to the phosphorylated opsin. GTPase-activating protein induces the a-subunit of transducin to hydrolyze its GTP to GDP. This inactivates phosphodiesterase, which in turn halts the conversion of cGMP to GMP.

All-*trans* retinal undergoes reduction to all-*trans*-retinol by retinol dehydrogenase. It is then transported to the retinal pigment epithelium (RPE). All-trans retinol is converted back to 11-*cis*-retinol by the isomerase RPE65 and then to 11-*cis*-retinal by 11-cis retinol dehydrogenase transported back to the photoreceptor outer segment.

Phototransduction Cone/Rod, Table 1 Involvement of phototransduction proteins in retinal disease

Affected protein (rod *or* cone)	Disease
Rhodopsin (rod)	ADRP, ARRP, CSNB
S-cone opsin (cone)	Tritan color vision defect
L-cone opsin (cone)	Protan color vision defect or BCM if both L and M opsins
M-cone opsin (cone)	Deutan color vision defect or BCM if both L and M opsins
Phosphodiesterase (rod)	ARRP, CSNB
Transducin (rod)	CSNB (Nougaret disease)
Transducin (cone)	Rod monochromacy (achromatopsia)
CNG channel (rod)	ARRP
CNG channel (cone)	Rod monochromacy (achromatopsia)
Rhodopsin kinase (rod)	CSNB (Oguchi disease), ARRP
Arrestin (rod)	CSNB (Oguchi disease), ARRP
Guanylate cyclase (both)	CRD, LCA
Guanylate cyclase-activating protein (both)	Cone dystrophy

Retinal Diseases Associated with the Phototransduction Cascade

Nearly every protein involved in the phototransduction cascade (including recovery and deactivation) has been associated with some form of retinal disease. A comprehensive list can be found at http://www.retina-international.org/sci-news/, though a subset is listed below in Table 1.

Cross-References

- ▶ Achromatopsia
- ▶ Atypical Retinitis Pigmentosa (RP)
- ▶ Bipolar Cells
- ▶ Night Blindness

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Photovideokeratoscopy

- ▶ Computerized Corneal Topography

Phthiriasis

▶ Pediculosis (Lice), Ocular Infection

Phthiriasis Palpebrarum

▶ Pediculosis (Lice), Ocular Infection
▶ Phthirus Pubis (Crab/Pubic Louse), Ocular Infection

Phthiriasis Pubis

▶ Phthirus Pubis (Crab/Pubic Louse), Ocular Infection

Phthirus Pubis (Crab/Pubic Louse), Ocular Infection

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Synonyms

Crab louse; Pediculosis ciliaris; Pediculosis pubis; Phthiriasis palpebrarum; Phthiriasis pubis; Pubic lice

Definition

Phthirus pubis, also known as pubic lice or crab louse, is a parasitic arthropod that infects, most commonly, human pubic hair. Infestation of the pubic hair is called pediculosis pubis or phthiriasis pubis. Transmission occurs through direct contact with an infected person or through shared use of linens. Via one of these mechanisms, phthirus pubis can also infect the eyelashes, which is called pediculosis ciliaris or phthiriasis palpebrarum. Ocular infection is usually bilateral and causes pruritis, burning, and irritation. Secondary conjunctivitis and preauricular adenopathy can also result.

Cross-References

▶ Conjunctivitis
▶ Ocular Lice
▶ Parasites
▶ Pediculosis (Lice), Ocular Infection

Physiologic Anisocoria

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Synonyms

Benign anisocoria; Central anisocoria; Congenital anisocoria; Essential anisocoria; Simple anisocoria

Definition

Physiological anisocoria is a non-pathologic difference in the size of the two pupils with normal light and near reflex reactions. The difference in size is typically less than 0.4 mm and almost never greater than 1 mm (Colby 2014). The disparity remains constant during constriction and dilation (Baloh and Jen 2012).

Basic Characteristics

Physiological anisocoria is the most common cause of anisocoria and occurs in about 20% of the population. Physiological anisocoria may be intermittent. It can vary from week to week and occasionally from hour to hour. It is considered to be a genetic or developmental phenomenon (Rucker 2012). Physiologic anisocoria tends to be equal in light and dark lighting conditions, the pupils are round, and the light and near responses are normal (Kanski 2011).

Diagnostics

Although generally not needed, some patients with physiologic anisocoria may require topical testing to exclude Horner syndrome.

Cross-References

- ▶ Anisocoria: Big Pupil
- ▶ Anisocoria of the Small Pupil
- ▶ Pharmacologic Anisocoria

References

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Phytochemicals

- ▶ Carotenoids (Xanthophylls)

Piggyback

- ▶ Piggyback Intraocular Lens

Piggyback Intraocular Lens

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Synonyms

Add-on intraocular lens; Piggyback; Supplementary pseudophakic IOL

Definition

Implantation of two or more intraocular lenses (IOLs) into the posterior chamber of the same eye.

Epidemiology

Due to its spectrum of indications for piggyback IOL implantation, this type of refractive surgery is performed infrequently.

History

Piggyback IOL implantation was first reported by J. Gayton in 1993. He implanted a pair of plano/convex PMMA IOLs with the plano surfaces opposed in a capsular bag/sulcus configuration in an eye with microphthalmos (Gayton and Sanders 1993). J. P. Gills was the next surgeon to perform piggyback implantation, reporting a series of eyes in which he implanted multiple PMMA IOLs in the capsular bag. In 1995, J. P. Gills showed surgical videos in which he implanted up to four IOLs into the same capsular bag in an effort to enhance depth of field. Application of foldable IOLs to piggyback implantation finally led to a marked increase of applications. Primary piggyback implantation was now also performed for additional indications, such as extending the power range for toric and multifocal IOLs (Gayton et al. 1999). The first case of piggybacking a multifocal IOL was presented in 1999. Today, secondary piggyback implantation evolves as a major modality for correction of pseudophakic refractive error in special situations such as extremely myopic, keratoconic, pediatric, and post-penetrating keratoplasty eyes (Mejía 1999).

Tests

In patients with small pupil diameter, diagnostic evaluation of the posterior chamber can be difficult with biomicroscopic examination. Anterior chamber imaging techniques like optical coherence tomography (OCT) or ultrasound biomicroscopy (UBM) are helpful to confirm status post piggyback IOL implantation (Baumeister and Kohnen 2006).

Differential Diagnosis

Interlenticular opacification may suggest a clinical aspect similar to IOL opacification.

Etiology

"Piggyback IOL" and "add-on IOL" are nowadays often used as synonyms. In the strict sense, the term "piggyback" means a primary implantation of at least two IOLs into the capsular bag of an aphakic eye, and the term "add-on" IOL stands for a secondary implantation of an IOL into the ciliary sulcus of a pseudophakic eye.

Treatment

According to the indications, there are three types of piggyback IOLs:

- Monofocal
- Multifocal
- Toric

The main concern of this type of surgery is the unique complication of the development of postoperative interlenticular opacification (ILO). The anterior surface of the anterior IOL adheres to the anterior capsule, and the posterior surface of the posterior IOL adheres to the posterior capsule preventing cell migration from the equatorial bow to the posterior capsule. This migration is directed to the interlenticular space. To avoid this complication, one should take care to remove lens epithelial cells completely during surgery to make the capsulorhexis larger than the IOL optic and prefer implantation of the posterior lens into the capsule and the anterior lens into the ciliary sulcus in order to avoid an interlenticular space that may support cellular ingrowth.

Cross-References

- ▶ Foldable Intraocular Lens
- ▶ Intraocular Lens
- ▶ Multifocal Intraocular Lens
- ▶ Posterior Chamber Phakic Intraocular Lens

References

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Pigment Epitheliopathy

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Synonyms

Acute multifocal placoid pigment epitheliopathy; Acute posterior multifocal placoid pigment epitheliopathy; Placoid pigment epitheliopathy

Definition

An acute disease of the choroid and pigment epithelium associated with placoid lesions, occurring in young otherwise healthy individuals.

Etiology

Unknown.

Acute posterior multifocal placoid pigment epitheliopathy is a rare eye disease presenting in otherwise healthy young individuals and may affect both genders equally. In most cases a flu-like illness precedes the onset of ocular symptoms and therefore a viral association was suggested.

A genetic predisposition may also be present with an association to HLA-B7 and HLA-DR2.

Numerous infections were described with association to APMPPE including mumps, streptococcus group A, tuberculosis, Lyme disease, and adenovirus type 5 infections.

An association with hepatitis B vaccination was also described.

A number of noninfectious systemic conditions have been reported in connection with APMPPE, including erythema nodosum, Wegener granulomatosis, polyarteritis nodosa, scleritis and episcleritis, sarcoidosis, and ulcerative colitis.

Several authors described central nervous system involvement ranging from headache in 50% of patients to rarely occurring cerebral vasculitis and even ischemic stroke.

These diverse associations may lead to the conclusion that APMPPE is associated with immune response.

Clinical Presentation

The typical clinical presentation of APMPPE is a sudden onset of painless visual loss, often bilateral with the fellow eye becoming involved within days to weeks. Some patients present with scotomas or metamorphopsia. In some patients, photopsias precede the visual loss.

On clinical examination, there are minimal signs of ocular inflammation with mild to moderate vitritis apparent in less then half of the patients.

Funduscopic findings include multiple, flat, creamy white placoid lesions at the level of the RPE and deep neurosensory retina, varying in size from 1 to 2 disc areas scattered throughout the posterior pole and the equator.

New peripheral lesions may appear in a linear or radial manner over the next few weeks with older lesions resolving within 2–6 weeks turning into permanent retinal pigmentary alterations.

Optic nerve head swelling may be present.

Atypical findings include retinal vasculitis, retinal vascular occlusions, macular edema, retinal neovascularization, and exudative retinal detachment.

A rare variant of APMPPE named relentless placoid chorioretinitis or ampigenous choroiditis has features of both APMPPE and serpigenus choroidopathy. The acute retinal lesions are similar to those seen in APMPPE but take a chronic relapsing course with appearance of new lesions and growth of subacute lesions up to 2 years after the initial presentation. Immunosuppressive therapy may be warranted in these cases.

Diagnosis

The diagnosis of APMPPE is based on the characteristic clinical presentation as well as imaging. Fluorescein angiography (FA) and indocyanine green angiography (ICG-A) were the mainstay of imaging modalities in APMPPE, but recently newer technologies such as higher resolution spectral domain optical coherence tomography (Sd-OCT) and fundus autofluorescence (FAF) are emerging giving additional insight regarding the pathophysiology of the disease.

FA findings during the acute phase of the disease include early hypofluorescence (blockage) of lesions corresponding to but typically more numerous than those seen on fundus examination. On late phases hyperfluorescence of the lesions due to staining is noted.

With resolution, various degrees of hyper- or hypofluorescence may be evident due to hyper- or hypopigmentation of the lesions (Fig. A).

ICG-A reveals choroidal hypofluorescence with hypervisualization of the underlying choroidal vessels in early and late stages of the imaging (Fig. B).

These findings may be seen during both acute and inactive stages of the disease with the lesions becoming smaller or resolving in the inactive stages.

Fundus autofluorescence (FAF) imaging show hypoautofluorescence in the area of the APMPPE lesions early in the disease, which then become hyperautofluorescent.

Sd-OCT of patients with AMPPE reveals a variety of abnormalities. The earliest phase seems to involve variable amounts of subretinal fluid with subretinal hyper-reflective material and rapid resolution of these subretinal lesions. Later in the disease course, lesions reveal either partial or complete restoration of the outer retinal architecture or may progress to thinning of the outer nuclear layer, disruption of the RPE layer, and atrophy.

There is still a controversy whether the lesions of APMPPE represent a primary involvement of the RPE or a choroidal perfusion abnormality with secondary involvement of the RPE and photoreceptors.

Nevertheless, taking the FA, ICG, and FAF imaging findings suggest a primary choroidal pathology with a secondary RPE and photoreceptors.

The choroidal perfusion abnormalities seen early on FA and ICG angiography are more numerous than the overlying placoid lesions seen on clinical examination; abnormalities noted on FAF imaging appear later and are fewer in number. All of these implicate a primary choroidal process.

Differential Diagnosis

Differential diagnosis includes:

Serpigenous choroidopathy
Multiple evanescent white dot syndrome (MEWDS)
Vogt-Koyanagi-Harada (VKH)
Persistent placoid maculopathy (PPM)

Prophylaxis

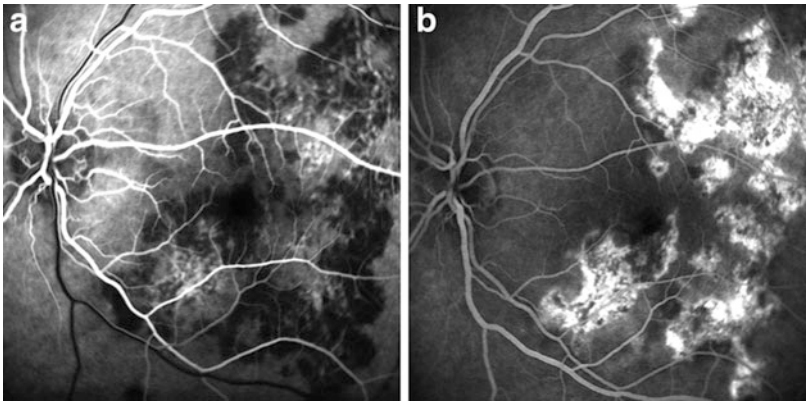
Unclear

Therapy

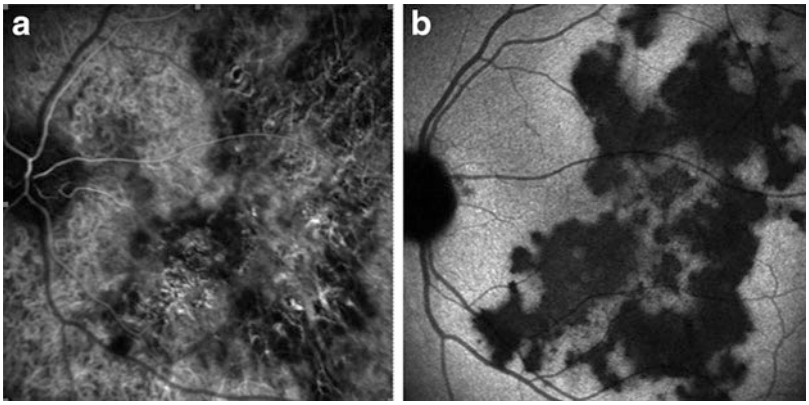
There are no prospective clinical trials regarding the value of treatment in patients with APMPPE. Nevertheless, reduced visual acuity, macular lesions, or CNS involvement are usually indications for systemic steroid treatment.

Prognosis

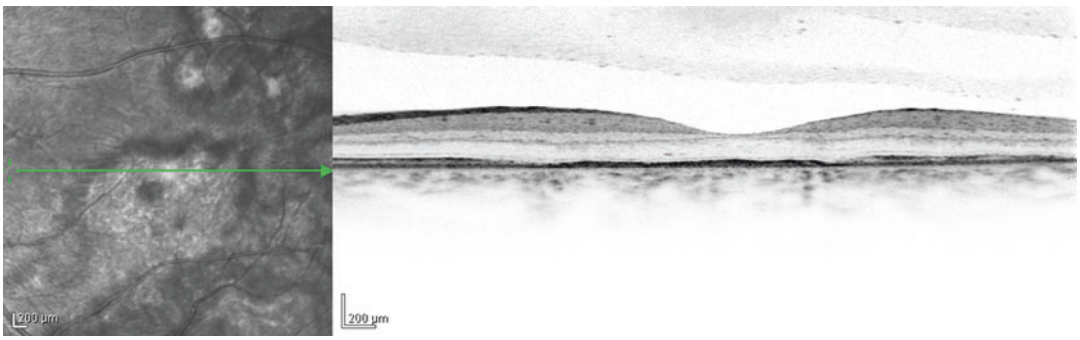
APMPPE is considered a relatively benign syndrome. Nevertheless, most patients have some reduction in visual function with 42% of eyes achieving a visual acuity of 20/40 or less.



Pigment Epitheliopathy, Fig. 1 (**a**, **b**) Early and late FA of a left eye in an 18-year-old patient with APMPPE demonstrate early hopofluorescence of the lesions with late hyperfluorescence



Pigment Epitheliopathy, Fig. 2 (**a**, **b**) Early and late ICG-A demonstrate hypofluorescence of the lesions in early and late frames



Pigment Epitheliopathy, Fig. 3 Sd-OCT demonstrates photoreceptor and RPE irregularities

Epidemiology

A single epidemiologic study reports an annual incidence of 0.15/100,000 Figs. 1, 2, and 3.

Cross-References

- ▶ Fluorescein, as Diagnostic Agent
- ▶ Indocyanine Green
- ▶ Optical coherence tomography

Further Reading

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Pigment Epithelium Detachment

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Synonyms

Detachment of the retina pigment epithelium

Definition

Retinal pigment epithelium detachment (PED) is a localized elevation of the retinal pigment epithelium (RPE) that loses its adherence from the underlining, inner collagenous layer of the Bruch's membrane. A PED can be found in a certain number of choroidal diseases as well as in some systemic conditions. Accordingly to the content, PEDs can be of various nature such as drusenoid, serous, vascularized, fibrovascular, and cellular. A drusenoid PED is occurring in a dry age-related macular degeneration (ARMD) and is secondary to the coalescence of drusen material in large agglomerates under the RPE. A serous PED is produced by the accumulation of fluid between RPE and Bruch's membrane; serous PEDs develop in several diseases like exudative ARMD, polypoidal choroidal vasculopathy (PCV), central serous chorioretiniopathy (CSC), choroidal inflammations, and various systemic and drug-related conditions. A third type of PED is the vascularized (hemorrhagic) PED that is generally associated with the ingrowth of neovascular choroidal vessels under the RPE (type 1 choroidal neovascularization) in exudative ARMD. A fibrovascular PED is an evolution of the vascular PED when the fibrous component predominates. A PED can also be cellular, due to the infiltration of the sub-RPE space by inflammatory or neoplastic proliferation. Finally, mixed types of PEDs can be found.

Etiology

The two main causes of PED are ARMD – and its variants polypoidal choroidal vasculopathy (PCV) and retinal angiomatous proliferation (RAP) – and central serous chorioretinopathy (CSC). However, even if less frequently, PEDs can be found in several systemic disorders of inflammatory, infectious, neoplastic, and iatrogenic nature (Table 1).

Inflammatory conditions include tubulointerstitial nephritis and uveitis syndrome and type II membranoproliferative glomerulonephritis. Other inflammatory conditions are inflammatory bowel disease, systemic lupus erythematosus, and sarcoidosis in which PEDs are often seen associated with neurosensory serous retinal detachments and subretinal fluids.

Infectious and immunologic causes comprehend pseudohistoplasmosis syndrome, choroiditis by *Blastocystis hominis*, poststreptococcal syndrome, and neurosyphilis.

Neoplastic conditions include Waldenström macroglobulinemia and multiple myeloma, where immunoglobulins accumulate under the RPE, and acute myeloid leukemia and large cell non-Hodgkin lymphoma, where neoplastic cells infiltrate the sub-RPE space causing the detachment. Even if rarely, choroidal nevi and

Pigment Epithelium Detachment, Table 1 Ocular and systemic conditions associated with PEDs

Ocular		Systemic			
Degenerative	Idiopathic	Inflammatory	Infectious	Neoplastic	Iatrogenic
AMD	CSC	Tubulointerstitial nephritis and uveitis syndrome	Pseudohistoplasmosis syndrome	Waldenström macroglobulinemia	Pamidronate
PCV	Small multifocal idiopathic PEDs	Type II membranoproliferative glomerulonephritis	Blastocystis hominis	Multiple myeloma	Corticosteroids
RAP		Inflammatory bowel disease	Poststreprococcal syndrome	Large cell non-Hodgkin lymphoma	Hemodialysis
		Systemic lupus erythematosus	Neurosyphilis	Acute myeloid leukemia	Organ transplantation
		Sarcoidosis		Choroidal nevi	
				Melanoma	

melanoma can be complicated by the development of a neovascular PED.

Among the drugs that promote the development of a PED are the pamidronate, a drug used to treat osteoporosis, and corticosteroids. Steroids are probably responsible of the PEDs seen in pregnancy and in organ transplantation with a mechanism similar to that seen in CSC.

Lastly, a condition characterized by the development of idiopathic, small, multifocal, and bilateral PEDs has been described.

Pathogenesis

The pathogenesis can be different depending on the type of PED. Drusenoid PEDs arise from the confluence of soft drusen, while the origin of serous and vascularized PEDs associated with the ARMD is not completely understood. A theory suggests that serous PED in ARMD is originated either from serous exudation from a hyperpermeable choroidal system through an intact Bruch's membrane or is secondary to fluid leakage from new vessels coming from the inner layers of Bruch's membrane into the subretinal pigment epithelium space (Gass 1984). According to another theory, aging promotes an increased deposition of lipids in Bruch's membrane that becomes hydrophobic and impermeable (Bird 1991). Thus, fluids would be unable to cross the diseased Bruch's membrane and accumulate into the sub-RPE space. A choroidal neovascularization (CNV) can be or not associated with PED.

Two peculiar forms of ARMD, namely, RAP and PCV, are associated with PEDs. RAP is a particular form of neovascularization involving both retinal and choroidal compartments that are anastomosed. RAPs are associated with vascularized PED that have a particular poor prognosis. The other form is the so-called PCV characterized by the development of extensive choroidal neovascular membranes growing between RPE and Bruch's membrane and ending with bulbar vascular dilations termed polyps. In PCV, wide and multiple vascularized PEDs that are frequently complicated by hemorrhages were developed.

PEDs in CSC are probably secondary to an abnormal choroidal circulation with hyperpermeable vessels. This is followed by increased hydrostatic pressure that forces the RPE to detach. The dysfunction of RPE leads fluids to cross into the subretinal space with development of an associated retinal detachment.

Clinical Presentation

PEDs associated with ARMD, both serous and vascularized, can cause reduction of visual acuity and distorted vision if they involve the macula. A hemorrhage within a vascularized macular PED

invariably causes an abrupt loss of vision. Serous PEDs associated with CSC have no influence on visual function if they are located outside the macular area. PEDs in the fovea can reduce or not visual acuity depending from the damage of the photoreceptor layer. Generally metamorphopsias and loss of vision in CSC depend on the associated serous retinal detachment.

Various types of PED have different ophthalmoscopic features. Drusenoid PED has the aspect of a pale yellow dome-shaped lesion under the RPE and is often surrounded by soft drusen. This lesion can be irregular and tend to be rather flat in some cases; pigment can be found on the top of the drusenoid detachment. Serous PED appears as a circular, yellow-orange elevation of RPE with well-defined borders. A vascularized PED can be indistinguishable from a serous PED only using ophthalmoscopy. Suspicious signs of a neovascular component are an irregular form and elevation of the serous PED and, more importantly, a notched border; the presence of subretinal exudates or hemorrhages, especially near the border of the PED, is pathognomonic of vascularization. When a large hemorrhage occurs in the vascularized PED, it acquires a dark brown color.

Diagnostics

The diagnosis of PED is greatly aided by techniques like fluorescein angiography, indocyanine green angiography (ICGA), fundus autofluorescence (FAF), and optical coherence tomography (OCT) (Mrejen et al. 2013).

Fluorescein angiography (FA). Drusenoid PEDs show a tenuous hyperfluorescence during the early phase of FA that slightly increases in the late phase. The serous PED displays typical features on FA examination. It shows early hyperfluorescence that increases due to the pooling into the detachment; the hyperfluorescence persists in later stages and can be attributed to staining of the fluid within the PED. FA is not always able to differentiate nonvascularized (serous) from vascularized PED; a choroidal neovascular membrane can sometimes be recognized as a hyperfluorescent lesion generally located near the borders of the PED. Generally, a vascularized PED shows a stippled hyperfluorescence that increases in later phases due to staining.

Indocyanine green angiography (ICGA). With ICGA examination the drusenoid PED is hypofluorescent and no hyperfluorescent areas are seen throughout the examination. ICGA shows the serous PED in ARMD as a hypofluorescent area both in the early and in the late phase (dark disk), secondary to a masking effect on the choroid from the fluid in the PED. However, ICGA frequently allows to distinguish serous PEDs from neovascular PEDs: the neovascular choroidal membrane appears as a hyperfluorescent circumscribed area generally seen as a notch in the border of the PED (hot spot) or a hyperfluorescent wide lesion standing out against the surrounding hypofluorescence (plaque). The first finding is a sign of active lesion, while the second is typical of quiescent neovascularization. In any case a hyperfluorescence of the PED in the late phase of ICGA is a sign of neovascular choroidal membrane. The ICGA findings in serous PED due to CSC are slightly different, since the PED in the mid-phase of ICGA acquires a hyperfluorescence due to choroidal hyperpermeability, and then, in later stages, it appears hypofluorescent with a characteristic hyperfluorescent ring.

Fundus autofluorescence (FAF). FAF is useful to demonstrate a PED, but has a very limited value in differentiating among the various types of PED. Drusenoid PEDs display various grades of hyperautofluorescence that can be irregular. Also serous and vascularized PEDs are hyperautofluorescent, with a hypoautofluorescent halo. The choroidal neovascular membrane is not recognizable with FAF.

Optical coherence tomography (OCT). OCT shows the PED as a prominence of the RPE detached from the underlying Bruch's membrane. In drusenoid PED this prominence can be irregular and the content hyperreflective, even if some areas can exhibit a less dense material; the pigment over the detachment is highly hyperreflective. In serous and vascularized PEDs, the borders of the lesion are neatly demarcated while the material inside the PED cannot be well appreciated in all the cases due to the limited ability of

OCT to penetrate the PED. A better resolution of the content of the PED is obtained with such OCT instruments or modalities that better explore deeper structures like the spectral-domain OCTs with the enhanced depth imaging (EDI) modality or the swept-source OCTs. A pure serous PED has a hyporeflective content, while the presence of hyperreflective material, especially adherent to the outer side of RPE, is suggestive of CNV. The evolution of a serous or vascular PED toward a fibrovascular PED is heralded by hyperreflective stratifications in the subretinal pigment epithelium space that represent the fibrous component of the detachment.

Differential Diagnosis

With ARMD being the first cause of PED, patient clinical history is fundamental for the diagnosis. The differential diagnosis among the various types of PED in ARMD is largely based on imaging techniques. In rare cases a brown elevation of RPE in the macular region could be suggestive of choroidal melanoma or subretinal pigment epithelium hemorrhage from various causes. FA, ICGA, OCT, and ultrasonography represent fundamental diagnostic tools.

Therapy

The therapy of PED in exudative ARMD is mainly based on the use of intravitreal injection of anti-VEGF drugs. These injections are performed as frequently as monthly even if many protocols are proposed, changing with experience. One of the most applied treatment consists in a loading phase of a drug, followed by further injections if any fluid is found with OCT examination; eyes treated in this manner show only a minimal reduction of visual acuity after 2 years and substantial reduction of the PED (Battaglia Parodi et al. 2013). However, despite the success of anti-VEGF drug treatments in drying the subretinal and intraretinal fluids associated with CNV, PEDs are often resistant to therapy, and in the long-term many eyes continue to show the PEDs as well as some extrafoveal subretinal fluid. Frequent injections of anti-VEGF drugs are associated with increased development and extension of geographic atrophy, so that the frequency of injections must be held at the minimum necessary to control the neovascular process.

Photodynamic therapy (PDT) with verteporfin was a standard treatment for exudative ARMD before the anti-VEGF era. It's still used today for patients with PEDs associated with PCV as well as in selected cases of exudative ARMD with extrafoveal lesions or choroidal vessels that can be localized by ICGA.

PDT combined with intravitreal injection of triamcinolone acetonide has been demonstrated to stabilize visual acuity and to decrease relapses of the PED. However, the use of intravitreal triamcinolone has been reduced for the high rate of complications like cataract and glaucoma that occurs with this treatment.

Prognosis

Drusenoid PEDs can persist more or less unchanged for years, but often evolve toward atrophy: the drusen-like material inside the PED reabsorbs, the detachment flattens, and atrophy of external retina follows. After a mean of 4.6 years, 28% of drusenoid PEDs persist, 49% evolve in geographic atrophy, and 13% develop choroidal neovascularization.

The evolution of serous PEDs in ARMD is various and, after 3 years, they can persist, flatten, or be associated with choroidal neovascularization with about a similar chance. A different evolution is seen in PEDs associated with CSC: they tend to flatten in most cases, leaving a slight pigmentary change, and persist in about one-third of cases.

Vascularized PEDs (i.e., a PED with sub-RPE neovascularization) have a relatively more benign prognosis than ARMD with subretinal neovascularization. However, a vascularized PED can evolve toward a hemorrhagic PED due to the bleeding from the choroidal neovascular membrane. Negative prognostic factors are the size of the vascularized PED, the turbidity of the

sub-RPE fluid, and the erosion of the RPE from the choroidal neovascular membrane that invades the subretinal space (type 2 neovascularization). Most of neovascularized PEDs complicated by hemorrhages develop disciform scars in a few months with resulting visual acuity below 20/200. The therapy with the injection of anti-VEGF drugs can halt the evolution of the vascularized PED. Especially after numerous intravitreal anti-VEGF drug injections, many PEDs evolve toward fibrovascular PEDs: the PED tends to flatten, the surface becomes corrugated, and the content becomes more dense with prevalence of fibrous component. A possible complication of PED, occurring in about 15% of cases, either spontaneously or following an injective therapy, is the tear of the retinal pigment epithelium.

RPE tears can be the cause of abrupt visual acuity drop in patients with exudative ARMD. Even if the pathogenesis of RPE tears is not completely understood, it is thought that an underlying choroidal neovascular membrane contracts, and the tangential shear forces cause dehiscence and separation of the epithelial basement membrane. Typical clinical features of this condition are RPE mounding and adjacent RPE atrophy. Potential risk factors for an RPE tear are a large-sized PED, central PED height, PED volume, presence of subretinal fluid, and long duration of treatment. In particular the severity of visual loss is correlated with the size and location of the tear: tears larger than 1 disk in diameter and those involving the fovea have bad prognoses. They are more likely to evolve with a severe vision loss and are least likely to respond to anti-VEGF therapy. On the other hand, small RPE tears located away from the fovea have better prognoses. If they are associated with subretinal fluid, vision may improve due to the positive response to following anti-VEGF therapy.

Epidemiology

PEDs are a frequent manifestation of ARMD and they are seen in up to 62% of eyes with advanced ARMD (Coscas et al. 2007).

Summary

The Pigment epithelium detachment (PED) is the separation of the retinal pigment epithelium from the Bruch's membrane, with the space between these layers filled with serous, vascular, fibrovascular or cellular material. The leading causes of PED are age-related macular degeneration and central serous chorioretinopathy. PED appears as a yellow, dome-shaped retinal elevation, better seen with the aid of fluorescein angiography and optical coherence tomography. The evolution of PED is variable and depends from its nature; the therapy is mainly based on the use of intravitreal injecton of anti-VEGF drugs.

Cross-References

- Age-Related Macular Degeneration
- Angiography, Fluorescein
- Central Serous Chorioretinopathy/Choroidopathy
- Indocyanine Green
- Optical Coherence Tomography
- Polypoidal Choroidal Vasculopathy
- Retinal Tears

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Pigment Epithelium, Ciliary Body, and Iris

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Definition

The pigment epithelium of the ciliary body is part of the double epithelial layer covering the ciliary processes and is contiguous anteriorly with the iris pigment epithelium and posteriorly with the retinal pigment epithelium.

The iris pigment epithelium is the posterior layer of the iris and is derived embryologically from neural ectoderm.

Structure

Each ciliary process is covered by a double epithelial layer which consists of an outer pigmented layer and an inner nonpigmented layer. The base of the pigmented epithelial cells faces the stroma of the ciliary process. The stroma contains vessels which provide water and ions for aqueous production. These molecules pass between pigmented epithelial cells and accumulate behind the tight junctions present between the nonpigmented cells.

The iris pigment epithelium consists of two layers (anterior cuboidal layer and posterior columnar layer) that are densely packed with melanin. The posterior layer is covered with a basement membrane that is continuous with the retina and ciliary body.

Function

The ciliary body pigment epithelium may have a minimal role in the blood aqueous barrier because of the presence of gap junctions between these cells and between the pigmented and nonpigmented epithelial cells of the ciliary body.

Clinical Relevance

The ciliary body pigment epithelium may be involved in reduction of intraocular pressure after transscleral cyclophotocoagulation for the treatment of glaucoma.

A ciliary body melanocytoma is a benign tumor that can directly invade angle structures and cause elevated intraocular pressure.

A ciliary body melanoma can be associated with high or low intraocular pressure, pigment dispersion, invasion of the angle by tumor, angle closure induced mechanically by the tumor, rubeosis irides, or neovascular glaucoma.

In pigment dispersion syndrome, contact of the posterior iris with the lens zonules causes atrophy of the iris pigment epithelium and the classic spoke-like mid-peripheral transillumination defects.

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Pigmentary Glaucoma

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Synonyms

Glaucoma associated with pigment dispersion syndrome (PDS)

Definition

Secondary open-angle glaucoma associated with PDS, an autosomal dominant disorder, in which irido-zonular friction disrupts the iris pigment

epithelium dispersing pigment granules throughout the anterior chamber.

Etiology

The underlying condition, PDS, can be explained by the anatomical phenomenon of posterior iris concavity, caused by reverse pupillary block due to increased irido-lenticular contact and physiological events such as blinking and exercise. Increased aqueous pressure in the anterior chamber promotes a backward bowing of the iris and mechanical rubbing against the zonular fibers of the lens leading to liberation of iris pigment. PDS is believed to be strongly influenced by genetic background with linkage to chromosomal locations 7q35-36 and 18q22.

Clinical Presentation

PDS is a bilateral disorder. Key features are the dispersion and accumulation of pigment on anterior segment structures such as the iris, lens, zonules, trabecular meshwork, and corneal endothelium, where it forms a characteristic vertical spindle-shaped pattern termed "Krukenberg's spindle." Gonioscopic examination of the chamber angle shows a dense, homogenous band of pigment in the full circumference of the trabecular meshwork. Radial, midperipheral, slit-like transillumination defects are typically present in the iris. The key signs of pigmentary glaucoma (PG) match those for PDS, but additionally involve elevated intraocular pressure, optic nerve head cupping, and visual field changes. Exercise may increase pigment dispersion and intraocular pressure in some patients.

Diagnosis

Classical diagnostic signs include the presence of a Krukenberg's spindle, wide-open chamber angle with dense trabecular pigmentation, and radial, slit-like, midperipheral iris transillumination defects on slit-lamp examination. Posterior iris concavity may be detectable by gonioscopy, ultrasound biomicroscopy, or anterior segment optical coherence tomography. Diagnosis of PG involves signs of glaucoma (elevated intraocular pressure, optic neuropathy, visual field loss) in the presence of PDS (Figs. 1 and 2).

Differential Diagnosis

Differential diagnosis of PDS and PG includes conditions associated with excessive pigment dispersion, such as pseudoexfoliation syndrome and pseudoexfoliative glaucoma, primary open-angle glaucoma, uveitis, ocular melanoma and melanocytoma, diabetic iridopathy, trauma, complications of ocular surgery, and age-related changes.

Prophylaxis

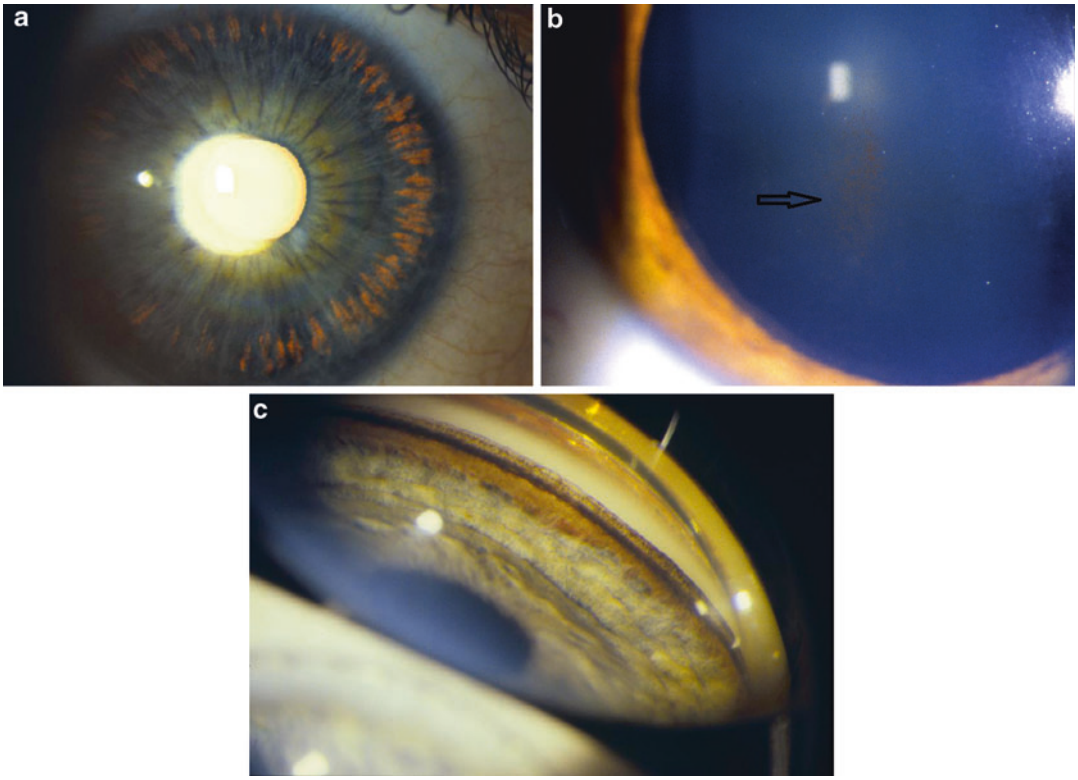
Laser iridotomy might be considered a prophylactic measure, but whether it can prevent the development of PG remains to be proven.

Therapy

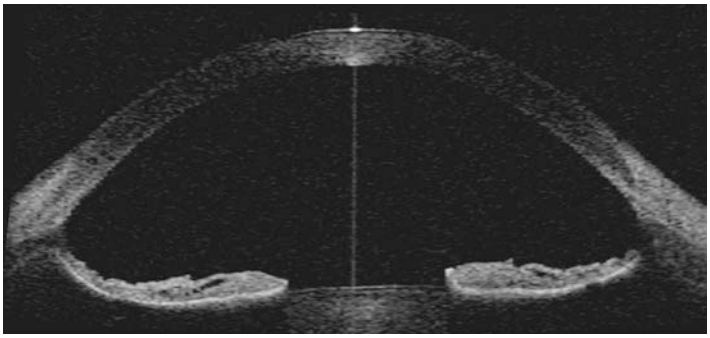
Treatment of PG follows the same regimen as primary open-angle glaucoma, but with some special considerations. Miotics not only lower intraocular pressure but also decrease irido-zonular contact and pigment liberation and may prevent further progression. Peripheral Nd:YAG laser iridotomy may be effective in eliminating reverse pupillary block, relieving the posterior iris bowing, and preventing pigment release in patients with marked iris concavity.

Prognosis

Prognosis is usually good and the majority of PDS cases do not progress to PG. PDS and PG tend to decrease in severity or become quiescent with advancing age due to exhausted liberation of pigment.



Pigmentary Glaucoma, Fig. 1 Clinical appearance of pigment dispersion syndrome. (**a**) Transillumination of the iris showing typical midperipheral slit-like defects. (**b**) Krukenberg's spindle (*arrow*) on the posterior surface of the central cornea. (**c**) Wide-open chamber angle with dense, homogenous pigmentation of the trabecular meshwork and iris concavity as viewed by gonioscopy



Pigmentary Glaucoma, Fig. 2 Typical iris configuration and increased irido-lenticular contact in a patient with pigment dispersion syndrome using anterior segment optical coherence tomography (Courtesy: R. Laemmer, Erlangen)

Epidemiology

PDS typically affects Caucasian individuals (about 2% of general populations). PDS is most commonly observed in female and male myopic patients 30–50 years old and PG is more prevalent in young myopic males. Approximately 20% of PDS cases have PG at initial diagnosis. The glaucoma conversion rate has been reported to be 10% at 5 years and 15% at 15 years.

Cross-References

- ▶ Primary Open-Angle Glaucoma
- ▶ Pseudoexfoliative Glaucoma
- ▶ Secondary Glaucoma in Uveitis

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Pigmentary Retinopathy

- ▶ Fundus Salt and Pepper

Pigmented Epithelial Lines

- ▶ Striate Melanokeratosis

Pigmented Lesions of the Conjunctiva

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Synonyms

Complexion-associated melanosis; Conjunctival melanoma; Conjunctival nevus; Primary acquired melanosis

Definition

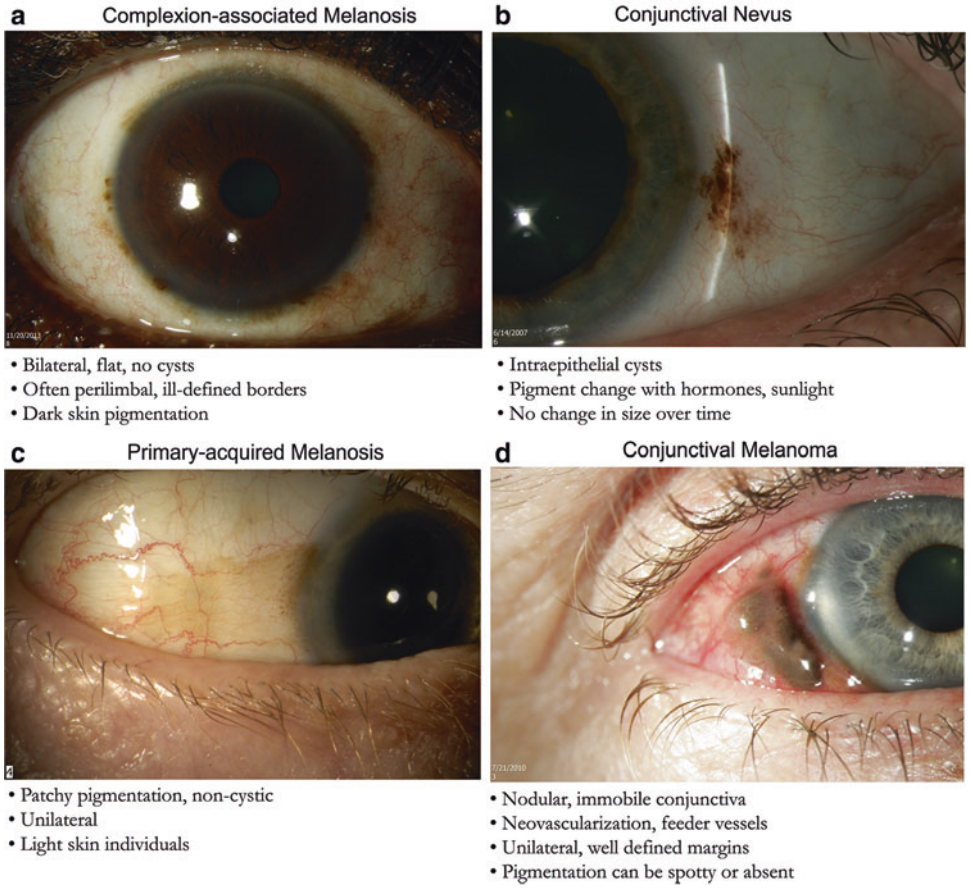
Pigmented tumors of the conjunctiva are comprised of four melanocytic lesions: complexion-associated melanosis, conjunctival nevus, primary acquired melanosis (PAM), and malignant melanoma (Harooni et al. 2011). Other lesions that can result in pigmentary changes visible on or through the conjunctiva include ocular melanocytosis and pigmented squamous cell carcinomas of the conjunctiva.

Etiology

- Complexion-associated melanosis is a result of hyperpigmentation of the conjunctival epithelium without any melanocytic proliferation. These lesions are usually seen in individuals with darker skin pigmentation. Historically, complexion-associated melanosis has often been referred to as "racial melanosis."
- Conjunctival nevi are derived from melanocytic proliferation and can be acquired or congenital. Pathologically they can be junctional, with melanocytes located at the junction of the epidermis and the dermis, and compound, in which melanocytes remain in the epithelium and have also infiltrated into the intradermal layers, or subepithelial, in which melanocytes are located only in the intradermal layers. Nevi are often characterized by cysts that can be seen clinically and pathologically. The cysts may grow, causing the nevus to appear to grow.
- Primary acquired melanosis (PAM) is a collection of melanocytes enclosed within the epithelium of the conjunctiva (Oellers and Karp 2012). Pathologic examination can reveal atypical cells within the lesion. The distinction between PAM with atypia and PAM without atypia is histologic and cannot be made clinically.
- Conjunctival melanoma is composed of malignant melanocytic cells. These lesions can arise from conjunctival nevi, from PAM with atypia, or de novo.

Occurrence

- Complexion-associated melanosis is common in individuals with dark skin pigmentation. There has been no reported incidence of this entity progressing to conjunctival melanoma.
- Conjunctival nevus is the most common pigmented conjunctival tumor, representing up to 52% of all conjunctival melanocytic tumors. It is most common in Caucasians (89%), but can occur in all races. The mean age at presentation is typically between the first and second decades of life. The rate of progression to melanoma is very low, up to 0.7% over 7 years.
- Primary acquired melanosis (PAM) is most commonly found in Caucasian adults but is seen in all races. The average age at presentation is between 50 and 60 years old. PAM without atypia has no malignant potential. Studies have shown that PAM with atypia can progress to malignant melanoma in 13–50% of cases (Oellers and Karp 2012; Shields and Shields 2004). In patients with severe atypia, rates of progression may be even larger.
- Conjunctival melanoma is uncommon, with a rate of 0.5 cases per one million in the United States. This represents only 5% of the melanomas of the ocular region. The average patient is middle aged (most in the fourth to seventh decade of life) and Caucasian (94% of all cases). However, conjunctival melanoma is seen in all ages (ranging from 10 to 91 years) and all races. Conjunctival melanoma is



Pigmented Lesions of the Conjunctiva, Fig. 1 Distinctive characteristics of the four major pigmented lesions of the conjunctiva

derived from PAM in 74% of cases, as a de novo malignancy in 21% of cases, and from nevus in 4% of cases. Metastatic disease occurs via lymphatic dissemination in up to 25% of patients with conjunctival melanoma after 15 years.

Classification

Given the malignant and metastatic risk of the pigmented conjunctival tumors, proper diagnosis is imperative. Some characteristics can help distinguish the lesions apart. Figure 1 outlines clinical characteristics suggestive of each entity.

Cross-References

- ▶ Complexion-Associated Melanosis
- ▶ Conjunctival Melanoma
- ▶ Conjunctival Nevus
- ▶ Melanosis Oculi
- ▶ Primary Acquired Melanosis

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Pilar Cyst

- ▶ Epidermal Cysts, of the Eyelid
- ▶ Sebaceous Cyst

Pilomatrixoma

- ▶ Lash Follicle, Tumors Arising in

Pilomatrixomas

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Synonyms

Calcified epithelioma of Malherbe

Definition

A rare, benign tumor originating from the matrix of the hair root.

Etiology

The exact etiology is uncertain; however, mutation in the gene encoding betacatenin (CTNNB1) has been described as a cause of tumor growth in the hair follicle. It can occur almost anywhere on the body but has a propensity to occur in the head and neck region, often involving the eyelid or eyebrow. It is most commonly seen in children and adolescents and with a female predominance (Albert and Jakobiec 2008; Levy and Ilsar 2008; Shields and Shields 2008).

Clinical Presentation

Typically presents as a solitary, firm, nontender, dermal or subcutaneous nodule, freely movable covered by normal, pink, or bluish skin. Usually slow growing over months or years but can occasionally exhibit rapid growth. Multiple pilomatrixomas have been observed, mainly in association with myotonic dystrophy (Albert and Jakobiec 2008; Shields and Shields 2008).

Diagnostics

Pilomatrixoma is often misdiagnosed clinically and the correct diagnosis only established after excision and histological examination. Histopathologically, this tumor is composed of ghost cells (shadow cells), basaloid cells, and calcium deposits (Albert and Jakobiec 2008; Levy and Ilsar 2008).

Differential Diagnosis

Differential diagnosis includes ▶ epidermal cyst, ▶ dermoid cyst, ▶ pyogenic granuloma, ▶ chalazion, ▶ sebaceous adenoma, ▶ basal cell carcinoma, ▶ keratoacanthoma, and ▶ hemangioma.

Prophylaxis

Unknown

Therapy

Surgical excision

Prognosis

Usually, this tumor has a benign course, although malignant transformations have been described (Shields and Shields 2008).

Epidemiology

Reported incidence varies widely in the literature; between 1:316 and 1:10,500 (Albert and Jakobiec 2008; Levy and Ilsar 2008; Shields and Shields 2008).

Cross-References

▶ Basal Cell Carcinoma of Eyelid
▶ Epidermoid Cysts
▶ Epidermal Cyst
▶ Keratoacanthoma
▶ Pyogenic Granuloma
▶ Sebaceous Adenoma

References

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Pinguecula

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Definition

A pinguecula is a common, elevated, nonmalignant growth of elastic tissue on the bulbar conjunctiva extending toward the limbus but sparing the cornea.

Etiology

It is believed that a pinguecula is a conjunctival degenerative change caused by actinic damage, particularly from ultraviolet (UV) radiation. The development of pingueculae is associated with aging, UV light exposure, and environmental traumas such as dust, wind, and sand. It is postulated that the nasal prevalence of pingueculae is from the reflection of UV light off the nose. The deposition of advanced glycation end products may be involved. These end reaction products of sugars and proteins can occur with UV radiation and the aging process, inducing oxidative stress

and molecular damage. Histologically, pingueculae are characterized as elastotic degeneration of subepithelial collagen with hyalinized connective tissue. In elastotic degeneration, tissue stains positively for elastin but is not degraded by elastase (Krachmer et al. 2011).

Clinical Presentation

A pinguecula presents as a yellow-white, elevated, avascular thickening of the bulbar conjunctiva adjacent to the limbus in the interpalpebral zone. The most common location is on the nasal side but may be seen temporally and is usually a bilateral phenomenon. The triangular-shaped thickening tapers in the direction of the angle of the eye. Calcification may be present. Patients are generally asymptomatic but may complain of irritation if the pinguecula is inflamed.

Diagnosis

Slit-lamp or external examination is the best way to diagnose pingueculae.

Differential Diagnosis

It is important to distinguish a pterygium from a pinguecula. A pterygium, while histologically similar to a pinguecula, is distinguished by fibrovascular tissue that grows onto the cornea. Pingueculae do not have vascularized tissue and do not cross the limbus. Dyskeratosis and epithelial tumors can be differentiated by their epithelial location compared to the subepithelial location of pingueculae.

Prophylaxis

Avoid UV light exposure and environmental traumas (sand, wind, and dust).

Therapy

Because pingueculae are slow growing, treatment is not usually necessary. Topical lubrication can be used to mitigate ocular irritation. Excision is rare but may be considered if cosmetically displeasing, chronically inflamed, exceedingly bothersome, or disruptive of contact lens wear. Inflammation of the pinguecula (pingueculitis) can occur and is treated with lubricants, topical corticosteroids, or topical nonsteroidal anti-inflammatory drugs.

Prognosis

Most pingueculae are asymptomatic and slow growing with little clinical significance. Uncommonly, there may be recurrent inflammation or irritation requiring further management.

Epidemiology

Pingueculae are the most frequent conjunctival change observed clinically. Prevalence increases with age. Pingueculae are seen very commonly in the eighth decade.

Cross-References

- ▶ Conjunctival Degenerations
- ▶ Pterygium

References

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Pink Eye

- ▶ Adenoviral Keratoconjunctivitis
- ▶ Conjunctivitis
- ▶ Haemophilus Influenzae, Conjunctivitis

"Pink Eye"

▶ Allergic Conjunctivitis

PIOL

▶ Phakic Intraocular Lens

PK

▶ Transplantation

Placido Disk

▶ Photokeratoscopy

Placido Ring

▶ Photokeratoscopy

Placoid Pigment Epitheliopathy

▶ Pigment Epitheliopathy

Planar Xanthoma

▶ Xanthelasma, Dyslipoproteinemia

Plate-Haptic IOL

▶ Plate-Haptic Posterior Chamber Intraocular Lens

Plate-Haptic Posterior Chamber Intraocular Lens

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Synonyms

Plate-haptic IOL

Definition

A plate-haptic posterior chamber intraocular lens is an IOL which has plate haptics that are positioned in the capsular bag or in the ciliary sulcus.

Epidemiology

Most IOLs available in the market are made of "loop" or "C" haptics.

History

The Staar plate-haptic IOL became the first FDA-approved toric IOL in 1998 (Hardten et al. 2003).

Clinical Features

Tests

Biomicroscopy in pharmacological mydriasis should reveal type of haptic.

Differential Diagnosis

A plate-haptic posterior IOL may be either an aphakic IOL (fixated in the capsular bag or the ciliary sulcus) or a phakic IOL (fixated in the ciliary sulcus or floating on the crystalline lens) and can be either toric or non-toric.

Etiology

IOLs with its optic and haptic made of the same material are termed "single-piece IOL," and IOLs with its optic and haptic made of different material are called "three-piece IOL" (Kohnen and Koch 2009).

Treatment

See also entries "▶ Cataract Surgery," "▶ Refractive Surgery," and "▶ Phakic Intraocular Lens" describing different IOL implantation techniques.

Cross-References

- ▶ Cataract Surgery
- ▶ Intraocular Lens
- ▶ Phakic Intraocular Lens
- ▶ Posterior Chamber

References

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Kohnen T, Koch DD (2009) Cataract and refractive surgery progress III, Essentials in ophthalmology. Springer, Berlin

Pneumatic Retinopexy

▶ Intraocular Gases

Pneumo-Orbitism

▶ Emphysema (Ocular), of Orbit and Eyelids, in Blowout Fractures
▶ Implants, Orbital

POBH

▶ Posterior Optic Buttonholing

Polyacrylic IOL

▶ Acrylic Intraocular Lens

Polydimethylsiloxane

▶ Silicone Oil Tamponade

Polymorphic Stromal Dystrophy

▶ Corneal Dystrophies

Polyorganosiloxane

▶ Silicone, Uses in Ophthalmology

Polypoidal Choroidal Vasculopathy

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Synonyms

Idiopathic polypoidal choroidal vasculopathy (PCV); Multiple recurrent serosanguineous retinal pigment epithelial detachments in Black

women; Posterior uveal bleeding syndrome (PUBS)

Definition

Polypoidal choroidal vasculopathy (PCV) is a macular disorder characterized by recurrent hemorrhage within the retina and retinal pigment epithelium (RPE). It is characterized by the presence of choroidal vascular channels (also known as the branching vascular network, BVN) ending in polyp-like dilations in the peripapillary and macular area.

Etiology

The etiology is still unknown. There are similarities between the genetic predisposition to PCV and to wet AMD. For example, a functional SNP at the promoter of serine protease HTRA1 was associated with a tenfold increased risk of developing PCV and choroidal neovascularization in Asians. Common causative genes include complement factor H on chromosome 1q23–32, albeit with different SNPs: Y402H (for neovascular AMD); rs3753394, rs800292 (for PCV); and HTRA2/ARMS2 on chromosome 10q26.

Clinical Presentation

The most common manifestations are submacular hemorrhage, hemorrhagic pigment epithelial detachment, serous pigment epithelial detachment, subretinal lipid exudates, neurosensory detachment, chronic central serous chorioretinopathy, and orange-red subretinal nodules (Fig. 1).

Diagnosis

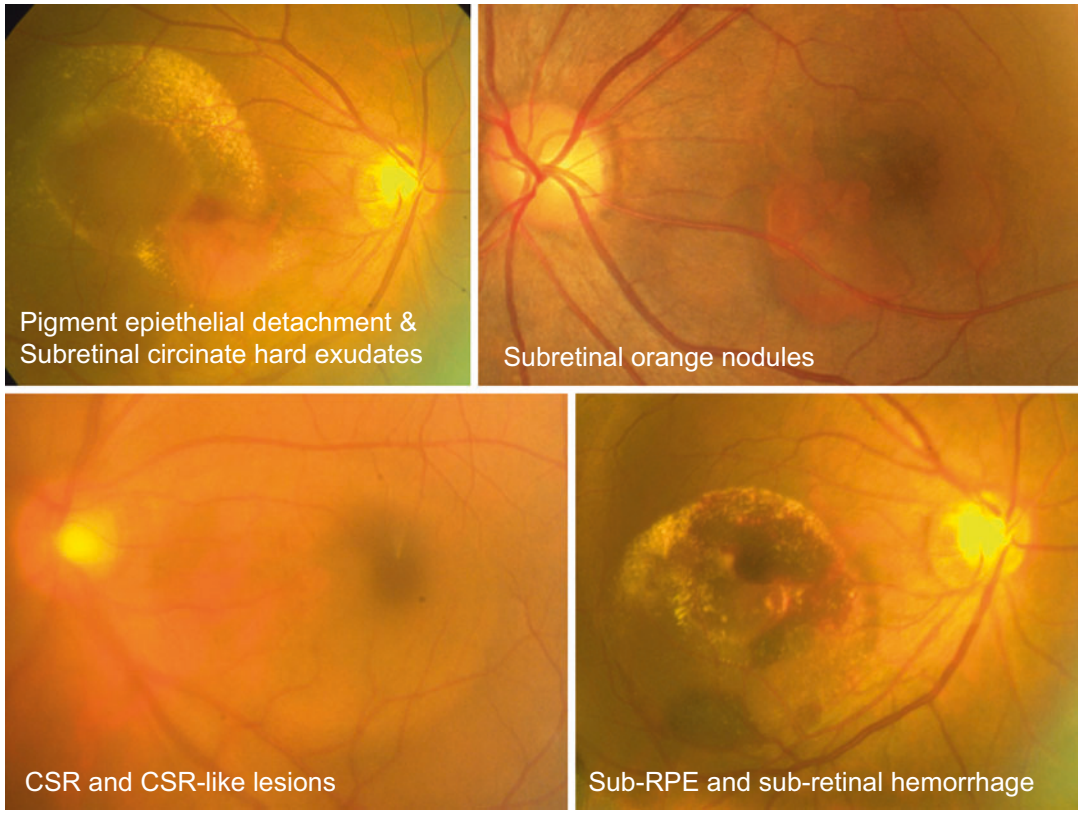
The most important diagnostic features are clinically visible orange sub-RPE polypoidal nodules and early nodular hyperfluorescence on stereo-ICG angiography. Spectral domain optical coherence tomography (OCT) is helpful in identifying these polypoidal nodules, which typically appear as sharply angulated inverted V-shaped elevation of RPE, lying between RPE and Bruch's membrane. The BVN appears as irregular undulation of RPE, with overlying and adjacent neurosensory detachment. Serous pigment epithelial detachments are frequently seen. Enhanced depth imaging is useful to differentiate PCV from CNV in AMD, because the choroidal thickness is typically increased in PCV due to choroidal congestion, especially where there is leakage on ICGA.

Fluorescein angiography is not diagnostic of PCV. The most common patterns are occult CNV, notched pigment epithelial detachment, hemorrhagic pigment epithelial detachment, and chronic central serous chorioretinopathy.

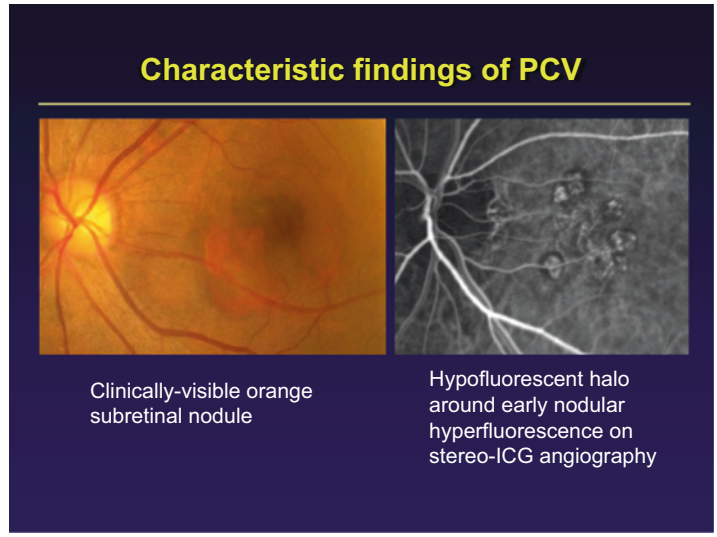
The gold standard of diagnosis of PCV is indocyanine green stereo-angiography (ICGA) (Koh et al. 686–716). The key features on ICGA are early focal nodular hyperfluorescence appearing within the first 5–6 min of the early phase of the angiogram. The plane of hyperfluorescence lies internal to large choroidal vessels, and these nodular structures protrude toward the observer and elevate the RPE layer. Other supporting features include a penumbra or halo of hypofluorescence surrounding the nodule in the early phase, followed by reversal of dye pattern in the late phase (20–30 min) due to staining of the walls of the structure, with the core having the dye emptied out, leaving an outer ring of hyperfluorescence surrounding central hypofluorescence (Fig. 2). In rare cases, pulsatility of the nodule can be observed on videoangiography, which is a pathognomonic feature of PCV that definitely differentiates it from CNV or RAP (Fig. 3).

Differential Diagnosis

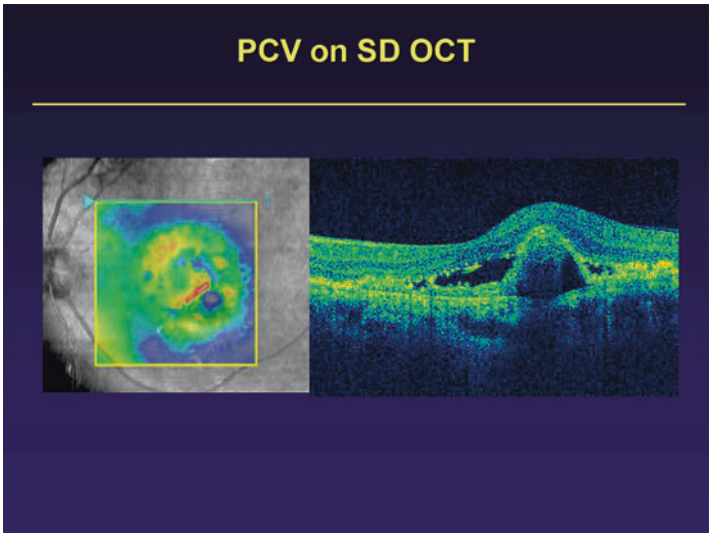
The most important differential diagnoses are occult choroidal neovascularization (CNV) and retinal angiomatous proliferation (RAP). Other entities to consider are central serous chorioretinopathy, retinal micro- or macroaneurysms, choroidal vascular knuckle, or RPE atrophy (Figs. 4 and 5).



Polypoidal Choroidal Vasculopathy, Fig. 1 Common clinical manifestations of PCV. The most common presentations of PCV are hemorrhagic pigment epithelial detachment, submacular hemorrhage, orange subretinal nodules, and neurosensory detachment

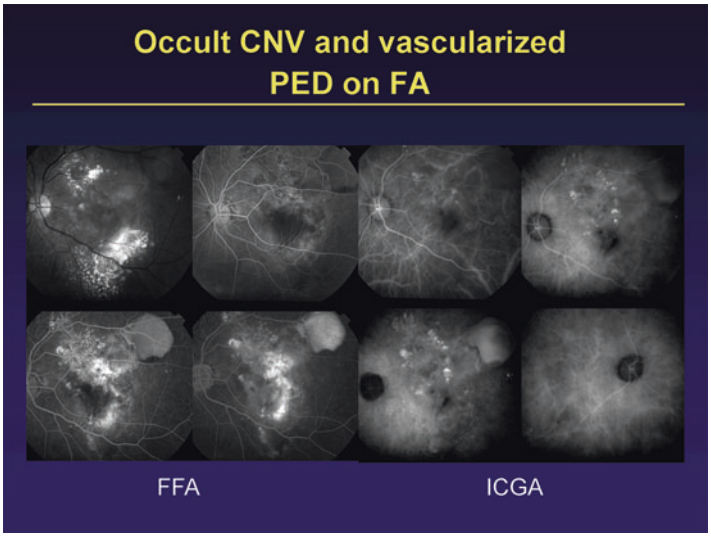


Polypoidal Choroidal Vasculopathy, Fig. 2 Characteristic findings of PCV. Orange subretinal nodules are seen in about 50% of cases on clinical examination but are almost pathognomonic of the condition. Indocyanine green angiography is the gold standard of diagnosis: a hypofluorescent halo surrounding early nodular hyperfluorescence within the first 5–6 min of the ICG is diagnostic



Polypoidal Choroidal Vasculopathy, Fig. 3 Spectral domain OCT findings in PCV. While ICGA is required for diagnosis of PCV, spectral domain OCT may be complementary by revealing sharp angular inverted V-shaped protrusions of the RPE, with surrounding pigment epithelial detachment and/or neurosensory detachment. Intraretinal edema is uncommon, unlike in retinal angiomatous proliferation (RAP), an important differential diagnosis. The polypoidal lesions lie between the RPE and Bruch's membrane. The branching vascular network may also be visible as irregular undulation or elevation of the RPE above the Bruch's membrane

Polypoidal Choroidal Vasculopathy, Fig. 4 Fundus fluorescein angiography is not diagnostic of PCV. Most PCV show occult patterns of leakage on the fluorescein angiogram. Another common finding is notched and hemorrhagic pigment epithelial detachments

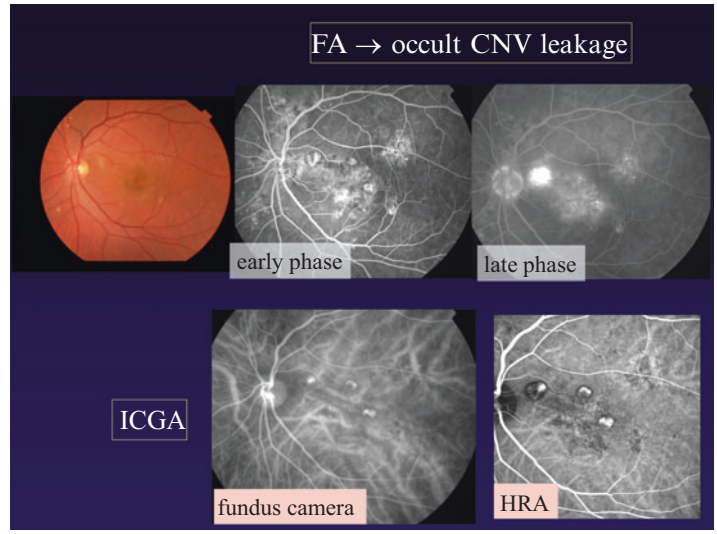


Prophylaxis

While there are no specific prophylactic treatments for PCV, AREDS-type supplementation may be given since PCV is considered a subtype of wet AMD.

Therapy

The primary goal of treatment in PCV, as in other subtypes of exudative AMD, is improvement or maintenance of vision. This can be achieved through the reduction and resolution of exudation



Polypoidal Choroidal Vasculopathy,
Fig. 5 ICGA features of PCV. The characteristic early nodule hyperfluorescence with a surrounding halo (penumbra) of hypofluorescence is diagnostic. In the later phases of the ICG angiogram, there is often a reversal of this pattern of fluorescence – central hypofluorescence with surrounding hyperfluorescence as the ICG dye leaches into the wall of the polypoidal lesion, and is washed out of its core

from the two components of PCV: the polyps themselves and/or the branching vascular network (BVN). Complete closure of polyps, confirmed on indocyanine green angiography, is a desirable secondary objective, especially in cases with persistent fluid at the macula despite multiple repeated ant-VEGF treatments due to active polyps. Furthermore, persistent polyps are associated with subsequent submacular hemorrhage, which may be massive and accompanied by severe visual loss, due to associated fibrosis and RPE atrophy (Figs. 6 and 7).

Options for therapy include the following:

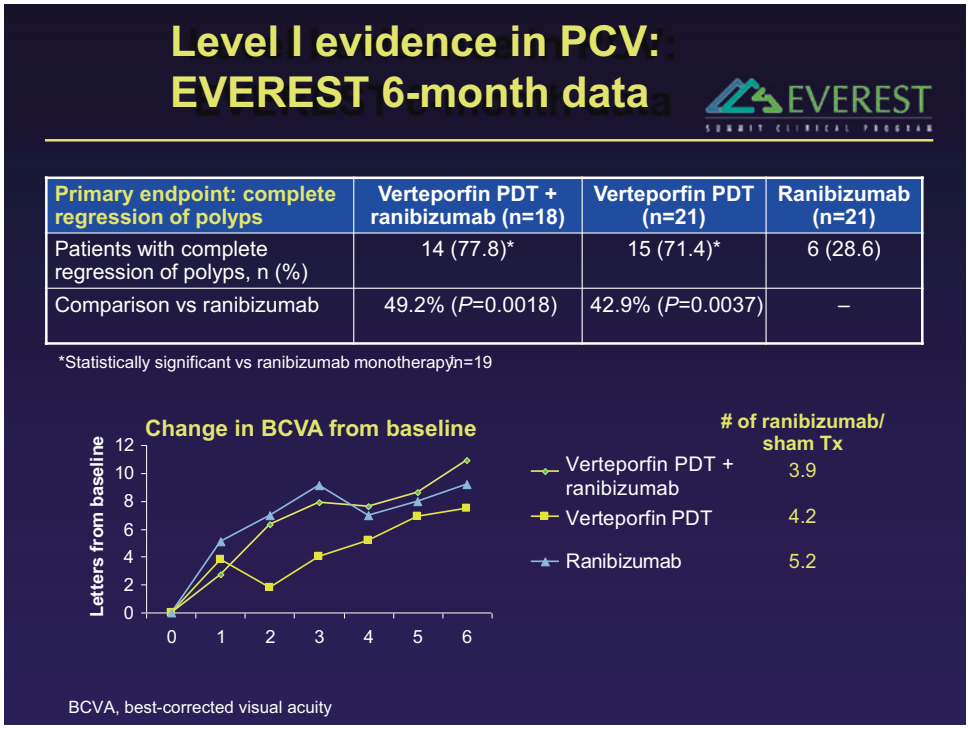
For extrafoveal PCV, focal ICG-guided laser photocoagulation may be used to occlude polypoidal lesions with moderate burn intensity. Chalky-white burns required to ablate choroidal neovascularization are not necessary. Recurrence rates are as high as 50%, and the subsequent lesions may be more extensive and hemorrhagic than the original. When lesions are subfoveal or juxtafoveal, the treatment options are verteporfin PDT (monotherapy), anti-vascular endothelial growth factor (VEGF) monotherapy, or verteporfin PDT-anti-VEGF combination therapy.

Laser Photocoagulation

Laser photocoagulation only has a role in ablating extrafoveal (preferably extramacular) polyps. Rarely, it may be effective in treating the entire complex of polyps with BVN which are extrafoveal. Limitations of laser photocoagulation include high rates of recurrences, formation of new lesions, enlargement of photocoagulation scars, tear or rip of the RPE, and iatrogenic choroidal neovascularization. Hence rates of visual loss as high as 45% have been reported following laser photocoagulation alone (Yuzawa et al. 2003).

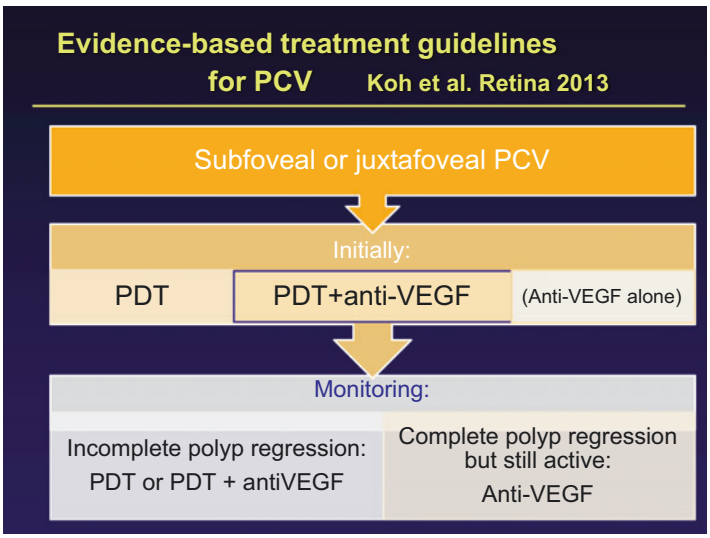
Verteporfin (Visudyne TM) Photodynamic Therapy

Verteporfin PDT has been shown to be effective in closure of polyps in PCV, but relatively ineffective in resolving activity arising from the BVN. Unlike CNV, treatment of PCV with verteporfin PDT results in mean improvement in visual acuity of eight letters at 12 months, with 25% of patients experiencing significant gains in vision of at least three Snellen lines; only 8% of patients in this prospective interventional study lost vision. 86% patients had cessation of fluorescein leakage at 1 year. Similarly, in the EVEREST trial, the mean change of visual acuity in the PDT-treated group was +7.5 letters at 6 months. The rate of complete closure of polyps was 71%, and that of partial but incomplete closure was 85.8% (Koh et al. 2012). Interestingly, the BVN seems more resistant to PDT treatment, with the majority of cases remaining unchanged despite repeated PDT. Another advantage of PDT is that the treatment-



Polypoidal Choroidal Vasculopathy, Fig. 6 The EVEREST study was part of the SUMMIT trials designed to evaluate the efficacy and safety of combination therapy of verteporfin PDT and ranibizumab in AMD and PCV. This is the first randomized controlled clinical trial to show that PDT, either alone or in combination with ranibizumab, was more effective than ranibizumab alone in complete regression of polyps at 6 months, with good visual acuity and OCT outcomes. The number of ranibizumab injections was the lowest in the combination group

P



Polypoidal Choroidal Vasculopathy, Fig. 7 Flowchart of clinical logarithm for treatment of PCV as proposed by the International Panel of PCV Experts

free period was significantly longer than was the case for CNV in AMD patients.

Studies comparing the visual outcome of PDT to anti-VEGF show that anti-VEGF therapy gives better visual results compared to PDT alone. This is because PDT is associated with complications such as acute vision decrease, increased subretinal hemorrhage, RPE tears, and, later, progressive RPE atrophy (Hirami et al. 2007). The major limitations of PDT monotherapy are reduction of vision in the long term, recurrence of polyps, persistence of BVN activity, secondary choroidal neovascularization (CNV), and progressive RPE atrophy. In 20–40% of cases, secondary CNV occurs within 2 years. Repeated full-fluence PDT gives rise to persistent choroidal ischemia, upregulation of VEGF, and RPE atrophy, all of which contribute to unsatisfactory long-term visual outcomes.

Anti-VEGF Monotherapy

The relative role of VEGF in the pathogenesis of PCV is variable: authors have shown no VEGF expression in the vascular endothelial cells of PCV, while one case report found strong expression of VEGF positivity in the vascular endothelial cells of PCV associated membrane. There were higher levels of aqueous VEGF in the eyes with PCV when compared to normal controls, albeit at lower levels than neovascular AMD.

Anti-VEGF therapy such as ranibizumab (Lucentis) and aflibercept (Eylea TM) is currently the gold-standard treatment for neovascular AMD, with significant rates of avoidance of moderate visual loss (over 95%) and doubling of visual angle (31%). This effect is maintained over three years. Ranibizumab monotherapy is also effective in achieving similar visual outcomes in PCV (Koh et al. 2012). Another indication for anti-VEGF therapy is for patients with good presenting visual acuity (e.g., 20/40 or better). Aflibercept has also been used to treat ranibizumab-tachyphylaxis in PCV cases. However, the polyp closure rate with bevacizumab and ranibizumab alone remains low. In the EVEREST trial, complete closure of polyps with ranibizumab therapy alone at 6 months was 28% compared to over 70% with verteporfin photodynamic therapy. In a retrospective study of three initial monthly injections of bevacizumab, only 1 out of 11 cases showed closure of polyps on the ICGA. Anecdotal evidence from VIEW 2 for probable PCV cases suggests a higher rate of polyp closure with aflibercept, but this remains unconfirmed. In addition, while anti-VEGF is effective in controlling exudation, the size of the BVN remained unchanged. What is undisputed, however, is the role of anti-VEGF therapy in treating activity of the BVN.

Combination Therapy: PDT with Anti-VEGF Agents

0There are good biologic and scientific rationales for combining verteporfin PDT with anti-VEGF therapy, in that both therapies employ different mechanisms of action which may be synergistic. While PDT is best for polyp regression, anti-VEGF is excellent at improving vision by reducing exudation from polyps and BVN activity. Anti-VEGF also mitigates post-PDT upregulation of VEGF through choroidal ischemia, thereby reducing the risk of acute vision decrease sometimes observed in PDT monotherapy, and might minimize the risk of post-PDT subretinal hemorrhage. EVEREST provided level 1 evidence in favor of PDT-ranibizumab combination in terms of polyp closure rate, number of ranibizumab treatments required, and equivalent short-term (6 months) visual outcome with ranibizumab alone (Koh et al. 2012). Similar results were observed in patients treated with PDT-bevacizumab combinations. The efficacy and safety of PDT with aflibercept have yet to be reported. Used together, the number of anti-VEGF injections can also be reduced. What is unestablished is the long-term visual results of combination therapy. Some studies suggest that while visual outcomes are good in the first 6–12 months, there is a significant drop-off into the second and third years.

Several authors have utilized modified PDT protocols such as reduced fluence PDT, in combination with anti-VEGF agents, with the aim of reducing the potential complications associated with PDT. These protocols have yet to be tested against conventional full-fluence PDT-anti-VEGF combination regimens. In recurrent cases, an important strategy might be to minimize the

laser treatment size by targeting only ICG-guided polyp lesions, rather than the entire lesion complex.

Optimal Treatment Regimens

There are several questions regarding optimal treatment regimens which remain unanswered. PCV may not respond to standard anti-VEGF monotherapy. While combination therapy may be an effective strategy, it is not clear if treatment should be concurrent or sequential. The use of initial anti-VEGF monotherapy might preclude the need for PDT and hence prevent related complications (Japanese guidelines recommend anti-VEGF monotherapy for patients with good VA [0.6–1.0]). Administration of anti-VEGF prior to PDT may allow more efficient delivery of the PDT laser to the consolidated target lesion; however, too long between anti-VEGFs and PDT might obviate the potential benefit that resolution of the exudation allows more efficient delivery of PDF laser to the consolidated target lesion. Efficacy appears better with anti-VEGF administered 2 days prior to PDT than 7 days prior to PDT. Concurrent (same day) administration of anti-VEGF agent and PDT means that PDT is applied when the anti-VEGF concentration peaks; this may counteract VEGF upregulation resulting from PDT-induced tissue hypoxia.

Other unresolved issues pertain to the need for three loading doses when combining therapies, which may be less important than for anti-VEGF monotherapy. There are also reported case series utilizing "triple therapy" comprising PDT, anti-VEGF with corticosteroids such as subtenon, or intravitreal triamcinolone. The author's own standard of care is to use reduced fluence ICG-guided PDT in combination with intravitreal anti-VEGF and dexamethasone. Controlled clinical trials will be needed to ascertain their true effectiveness.

Re-treatment criteria should be based on disease activity: reduced visual acuity, macular thickening from fluid, leakage from polyps, and/or BVN. Treatment modality will then depend on which is the predominant cause: persistent polyps should be selectively treated with PDT in combination with anti-VEGF, while activity from BVN alone should be managed using anti-VEGF monotherapy, since PDT has little effect on the activity or size of the BVN and might accelerate RPE atrophy and photoreceptor cell loss. The objective in re-treatment is to minimize complications from PDT, by reducing the frequency, spot size, and possible fluence.

Prognosis

The disease generally follows a remitting and relapsing course, with spontaneous remissions in between episodes of serosanguineous maculopathy. About half (50%) of patients are expected to suffer moderate or severe visual loss over 5 years. The main causes of poor vision in PCV are fibrosis and disciform scarring, RPE and neuroretinal atrophy, cystic degeneration, breakthrough vitreous hemorrhage, and, rarely, massive suprachoroidal hemorrhage and phthisis bulbi.

Epidemiology

There is a clear predilection for patients of Oriental Asian and Afro-Caribbean origin. The prevalence of PCV in Oriental Asian races such as Chinese, Japanese, and Korean ranges from 20% to 50% of all cases presenting as exudative maculopathy, compared to 8–10% in Caucasian White people. There is no significant gender predilection. Age of presentation is almost a decade younger than typical AMD. In addition, bilateral disease is found in only about 20% of cases, compared to about 50% of neovascular AMD over 5 years.

Cross-References

- ▶ Age-Related Macular Degeneration
- ▶ Antivascular Endothelial Growth Factor
- ▶ Choroidal Neovascularization

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Polysiloxane

► Silicone, Uses in Ophthalmology

Porosyringoma

► Hidradenoma, Clear Cell (Eccrine Acrospiroma)

Port-Wine Stain (Nevus Flammeus)

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Synonyms

Hemangioma; Nevus flammeus; Strawberry mark; Vascular nevus

Definition

A port-wine stain refers to a congenital angioma and is named as such due to the deep red hue rising from its vascularity. Found most commonly on the face, these grow proportionately with the body and darken over time from a pink to red-purple tone. Distribution is typically unilateral and respects the vertical midline. Facial lesions are typically distributed along the pattern of a branch of the trigeminal nerve, but frequent the forehead and upper eyelid, and hemihypertrophy of the face may develop. Oral lesions are present in 25% of patients. Port-wine stains represent a classic feature of Sturge-Weber Syndrome, a phakomatosis with cutaneous, central nervous system and ocular abnormalities, in which ocular findings include glaucoma, abnormal plexus of episcleral vessels, iris or optic nerve coloboma, tortuous retinal vessels, and choroidal angioma.

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Port-Wine Stain (Nevus Flammeus) in Sturge-Weber Syndrome

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Definition

A port-wine stain (PWS), or nevus flammeus, is a type of birthmark caused by a capillary

malformation in the skin. It is present at birth and typically grows in proportion with the child. Commonly occurring on the face, it can be a sign of a phakomatosis, Sturge-Weber syndrome (SWS), a congenital neurological and skin disorder that also includes abnormal blood vessels on the surface of the brain (ipsilateral cerebral leptomeningeal vascular malformations), and subsequent neurologic complications.

Differential Diagnosis

The presence of a PWS is not sufficient for the diagnosis of Sturge-Weber syndrome, and many cases of PWS are sporadic and isolated. In addition to SWS, however, other potential differential diagnoses include nevus simplex, infantile hemangioma, arteriovenous malformation, and linear scleroderma.

Diagnosis

The diagnosis of a PWS is made clinically. In order to diagnose SWS, leptomeningeal capillary-venous malformations should also be present. A cranial magnetic resonance imaging (MRI) with contrast is typically used to detect the presence of these malformations in the brain.

Pathogenesis

The pathogenesis of capillary malformations is unknown. Several mechanisms such as vascular ectasia, lack of neuronal control of blood flow, and the overexpression of vascular endothelial growth factor (VEGF) are thought to be involved.

Individuals with SWS possess somatic mosaic mutations in the CNAQ gene. This gene encodes a guanine nucleotide-binding protein that functions to regulate intracellular signaling pathways. Individuals who develop the CNAQ mutation earlier in development are more likely to acquire SWS, whereas individuals who acquire the mutation much later may only have a port-wine stain and no other complications.

Clinical

The PWS can occur anywhere on the body, though they are commonly found on the face and tend to follow the distribution of the trigeminal nerve branches. These lesions may extend onto the mucosal surfaces inside the mouth.

One of the most serious complications of a PWS-related capillary malformation is ocular involvement and secondary glaucoma. The development of glaucoma is believed to be caused by elevated episcleral venous pressure secondary to the obstruction of venous drainage around the eye.

If the patient has SWS, additional neurologic complications include early onset seizures in childhood, hemiparesis contralateral to the affected side of the brain, intellectual disability, and behavioral problems.

Treatment

Medical therapy for SWS includes anticonvulsants for seizure control, symptomatic and prophylactic therapy for headache, and intraocular pressure lowering agents and possibly laser therapy for glaucoma and laser treatments for the PWS. Epilepsy surgery may be necessary for medically refractory seizures, and glaucoma surgery is often needed for refractory glaucoma in SWS.

Prognosis

The prognosis for SWS depends on the extent of the leptomeningeal capillary-venous malformation and to what extent it effects perfusion of the cerebral cortex. The prognosis of the PWS depends upon its extent of ocular involvement.

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Poser Criteria, for Multiple Sclerosis

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Synonyms

Clinically definite MS; Multiple sclerosis diagnosis

Definition

The Poser criteria are a set of diagnostic parameters determined by Charles Poser et al. in 1983 for the diagnosis and classification of multiple sclerosis (MS) (Poser et al. 1983). The four categories are clinically definite, laboratory-supported definite, clinically probable, and laboratory-supported probable multiple sclerosis (Poser et al. 1983). The purpose of deriving these criteria was to establish a reliable diagnostic definition of MS for research studies that incorporated both clinical evidence and laboratory data (Poser et al. 1983). The Poser criteria replaced a previous scheme that did not analyze laboratory data but has since been replaced by a newer method that incorporated a greater role for magnetic resonance imaging (MRI) (Fangerau et al. 2004; McDonald et al. 2001; Poser et al. 1983).

Under the Poser criteria, patients are classified into one of the four categories based on number of clinical attacks lasting more than 24 h they have had, number of separate lesions evoking clinical signs, supportive imaging studies or physician assessments (termed paraclinical evidence), and the presence of oligoclonal bands in the cerebrospinal fluid (CSF) (but not in the serum) plus an increase in CSF immunoglobulin G (Poser et al. 1983). Clinically definite MS requires two attacks with clinical or paraclinical evidence of two distinct lesions (Poser et al. 1983).

Poser's definitions do not allow for the classification of primary progressive MS or for the effective utilization of magnet resonance imaging. Newer MS criteria include the McDonald criteria which were published in 2001 and revised in 2005 and 2010 (McDonald et al. 2001; Milo and Miller 2014; Poser et al. 1983).

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Positron Emission Tomography

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Definition

Positron emission tomography (PET) is a type of functional imaging which uses positron-emitting radiopharmaceuticals which, when emitted, will travel a few millimeters before encountering an electron in the surrounding area resulting in complete annihilation. The annihilation results in simultaneous emission of two gamma photons in opposite directions. These rays are received by the surrounding detector simultaneously at two different points (electronic coincidence) inferring that the decay took place somewhere along the line between the two simultaneously detected events. A great number of these events are recorded in order to produce a 2D horizontal cross-section image. Many of these images are collected and reconstructed to form a functional 3D image.

Like SPECT (see "► Single-Photon Emission Computed Tomography"), PET is a type of functional imaging and does not yield the most beneficial image of the anatomical features of the viewed area as in conventional structural imaging (e.g., CT or MRI). As a result, PET is often combined with conventional x-ray-based structural computed tomography (CT) for simultaneous functional and anatomical imaging. Thus this PET/CT dual-modality imaging results in increased speed, accuracy, and convenience allowing a physician to look at both the functional and anatomical/structural features of patients.

History

A few years after development in 1949 and early clinical use of a planar gamma-ray scanning device, a positron-annihilation imaging scanner was developed for use on human patients as early as 1956. The early positron-annihilating systems used opposing pairs of small detectors similar to today both with and without the use of electronic coincidence.

Basic Mechanism

Radiopharmaceuticals labeled with positron-emitting radioisotopes are injected into a patient who has been placed in an area surrounded by gamma-ray detectors. After traveling a few millimeters within the body, the positrons, which are emitted from the decaying radioisotope nuclei, encounter electrons in the surrounding area. These particles annihilate upon colliding, emitting two gamma photons in opposite directions. These two photons are collected by gamma-ray detectors which can infer the origin of the decay event, based on the premise that the emitted gamma rays traveling directly opposite each other will be detected simultaneously (electronic coincidence). Collected photon events pass through

amplifiers and a pulse-height analyzer to determine which events have high-enough energy signals for further analysis. These events are then analyzed for electronic coincidence to observe from where in the body various photons arose. An image is then reconstructed from the summation of points between two coincidental events from the many pairs of photons.

Clinical Uses

PET scans are used commonly to detect aberrant metabolic activity which may be indicative of cancer. PET can be used on lymph nodes to detect abnormal activity even prior to swelling, and it may be used on the heart to observe adequate blood flow and potential coronary artery disease. It can also be used as a diagnostic for brain disorders (e.g., Alzheimer disease, posterior cortical atrophy, epilepsy).

Comparison with SPECT

PET does produce images with higher resolution; however, availability for SPECT is more accessible due to the affordability and lower priced radiopharmaceuticals. PET system development may continue to lower the cost and increase the accessibility of the system. PET remains the preferred functional imaging method for research due to its high resolution.

PET/CT dual-modality imaging for oncological purposes has gained a great deal of clinical approval. In recent years, oncology clinics have been encouraged to replace stand-alone PET systems with dual-modality systems. In comparison, SPECT/CT dual-modality systems have not succeeded in the same way as there are lower clinical indications for this specific combined procedure.

Cross-References

► Single-Photon Emission Computed Tomography

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Posner-Schlossman Syndrome

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Synonyms

Glaucomatocyclitic crisis

Definition

Posner-Schlossman syndrome (PSS) is a rare form of recurring and remitting IOP elevations with associated/secondary mild inflammation.

Etiology

The clinical picture has been described and named by Posner and Schlossman in 1948 after the first reports by Kraupa in 1924. Not much is known about the etiology, although a possible role of herpes virus, especially CMV, has been postulated (Chee and Jap 2008). Reduction in aqueous outflow facility due to inflammation as well as augmented levels of prostaglandins leading to increased aqueous humor production has been reported. Some studies have even suggested an association with primary open-angle glaucoma (Mudumbai and Salim 2010). Most studies date

Friederike Mackensen: deceased.

back to the 1960s and 1970s with more recent publications linking PSS with non-arteritic anterior ischemic neuropathy (Irak et al. 2003).

Clinical Presentation

The pressure rise is typically unilateral and affects young to middle-aged individuals. The rise of IOP is out of proportion to the severity of the uveitis, up to 60 mmHg, and this rise in IOP precedes the identifiable inflammatory reaction, often by several days. The patient notes mild ocular discomfort and blurred vision of sudden onset. On examination mild iridocyclitis is seen with few cells and flare, with corneal edema and typical nonpigmented small- to midsized keratic precipitates in the center and lower half of the cornea that do not resemble the keratic precipitates seen in other uveitic entities. No synechiae formation is observed. The attack is usually short-lived and responds well to topical corticosteroids and carboanhydrase inhibitors topically and/or orally. Between attacks both the anterior chamber inflammation and IOP return to normal without the need of ongoing treatment (Grehn and Mackensen 1993; Mudumbai and Salim 2010).

Diagnosis

So far the diagnosis is a clinical one. It is important to recognize the clinical picture and educate the patient accordingly.

Differential Diagnosis

The differential diagnosis of PSS includes other conditions with unilateral raised IOP such as Fuchs uveitis syndrome (FUS) and herpetic uveitis or pigment dispersion syndrome. Iris hypochromia has been described already by the first describers as well as iris atrophy. The main distinguishers to FUS are the appearance of KPs, corneal, especially endothelial edema, flare in the anterior chamber, the patient describing symptoms, and the good response to topical corticosteroids. An FUS patient usually develops a pressure rise over time, not as a sudden occurrence. Herpetic uveitis usually shows pigmented granulomatous KP with more associated inflammation and needs more intensive and prolonged treatment. Gonioscopy finding of a normal angle structure helps in distinguishing pigment dispersion syndrome.

Prophylaxis

In between attacks treatment neither for glaucoma nor uveitis is needed nor would it prevent recurrences. In rare cases, the long duration of disease development of glaucoma has been described. Most important is to counsel the patient regarding his or her disease and educate them to seek appropriate care in the case of an acute attack.

Therapy

Topical corticosteroids are given to control inflammation. IOP in most cases normalizes with this treatment alone. Additional antiglaucomatous drops may be needed. Surgical treatment is only needed exceptionally. In cases where CMV is involved, ganciclovir can be considered, but relapse after cessation of treatment is frequent.

Prognosis

Prognosis is relatively good.

Epidemiology

PSS is extremely rare. It was seen in only 10 out of 1916 patients in a German tertiary center (Jakob et al. 2009). Looking at the literature published, it seems to be more frequent in Singapore than in other countries, where 74 presumed PSS patients of mostly Chinese race were seen in a 2-year period (Chee and Jap 2008). A mild male preponderance has been described.

There is some difficulty regarding the somewhat soft clinical definition which will have to be

sorted out, e.g., clarifying if CMV-associated uveitis should not be regarded as a uveitis entity different from PSS.

Cross-References

- ▶ Fuchs Heterochromic Iridocyclitis, Glaucoma
- ▶ Fuchs' Uveitis Syndrome (FUS) with Secondary Glaucoma
- ▶ Glaucoma Associated with Pigment Dispersion Syndrome (PDS)
- ▶ Stromal Keratitis (Herpetic)
- ▶ Uveitic Glaucoma

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Postcontusion Glaucoma

- ▶ Angle Recession Glaucoma

Posterior Amorphous Corneal Dystrophy

- ▶ Amorphous Corneal Dystrophy, Posterior Disease

Posterior Blepharitis

- ▶ Chalazion
- ▶ Seborrheic Blepharitis

Posterior Capsule Opacification (PCO)

- ▶ Capsular Bag Opacification

Posterior Capsule Rent

- ▶ Posterior Capsule Rupture

Posterior Capsule Rupture

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Synonyms

Posterior capsule rent; Posterior capsule tear

Definition

Posterior capsule rupture is defined as any breach in the integrity of the posterior capsule. Reason for this breach can either be congenital/traumatic (preexisting), spontaneous, or intrasurgical.

Epidemiology

Intraoperative capsule ruptures are the most common. They may occur accidentally or may be

planned, as in a primary posterior capsulorhexis. Between 1983 and 1997, the intrasurgical complication rate was reported between 1.5% and 11.4% dependent to the surgical technique, skill of surgeon, and stage of cataract. The incidence of intraoperative/traumatic posterior capsule tear has been reported to be higher in developing countries because of limited resources and delayed treatment, resulting in more advanced pathology. Spontaneous ruptures of posterior capsule tear are rare.

History

No detailed information exist about the history of posterior capsule rupture.

Clinical Features

Posterior capsule (PC) rupture during phacoemulsification cataract surgery remains an important complication because it may lead to poor visual outcome. Vitreous loss can occur in posterior capsule rupture and is associated with various complications including cystoid macular edema, glaucoma, retinal detachment, and infective endophthalmitis.

Tests

Visit with check of uncorrected and best corrected vision acuity and slit lamp examination with dilated and undilated pupil are important examinations to test the presence of a posterior capsular rupture.

Differential Diagnosis

Posterior polar cataract

Etiology

Intraoperative capsule ruptures may occur accidently or may be planned, as in primary posterior capsulorhexis. An increased intrasurgical capsule rupture rate is reported in patients with diabetes mellitus and pseudoexfoliation. Posterior polar cataracts, posterior lenticonus, cataract with persistent primary hyperplastic vitreous, and cataract following vitreoretinal surgery have also demonstrated increased propensity for the occurrence of posterior capsule rupture. Spontaneous capsule rupture is associated with hypermaturity, posterior lenticonus, intraocular tumors, and posterior polar cataracts. Traumatic capsule rupture can be caused by ocular or orbital injuries, and congenital posterior capsule rupture is related to posterior polar or infantile hypermature cataract. Intrauterine insults may be possible for both congenital cataract and congenital posterior capsule rupture.

Treatment

Prompt diagnosis and meticulous management are mandatory to prevent further enlargement of the tear and avoid consequent complications. The conventional management consists of prevention of mixture of cortical matter with vitreous, dry aspiration, and anterior vitrectomy, if required. In addition, during phacoemulsification low flow rate, high vacuum, and low ultrasound are advocated if a posterior capsule tear occurs. Dislocated nucleus or nuclear fragments require vitrectomy and the use of perfluorocarbon liquids. In the presence of a posterior capsule tear, the IOL can be placed in the sulcus, if the capsular rim is available, or in the bag, if the tear is small. Scleral fixated posterior chamber lenses and anterior chamber IOLs can be implanted when the posterior capsule tear is large. For prevention of posterior capsule rupture, viscodissection was reported to be a successful method.

Cross-References

▶ Lenticonus
▶ Primary Posterior Capsulorhexis

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Posterior Capsule Tear

► Posterior Capsule Rupture

Posterior Capsulorhexis

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Synonyms

Posterior capsulotomy; Posterior continuous circular capsulorhexis (PCCC)

Definition

A step of cataract surgery used in pediatric patients to avoid a late posterior capsule opacification. In adults, this technique is practiced in the presence of a central posterior capsular tear, posterior polar cataract, or in primary posterior capsular opacification.

Epidemiology

See "Epidemiology" section of "► Cataract Surgery" entry.

History

See "History" section of "Capsulorhexis" entry.

Clinical Features

Conducting instruments are either a cystotome or a bended needle.

Tests

See section "Tests" of "► Cataract Surgery" entry.

Differential Diagnosis

Another technique which is commonly applied is the continuous curvilinear capsulorhexis (CCC).

Other capsular opening methods in the following are, for example:

- Can-opener technique (letter-box technique): traditionally used in pediatric cataract surgery, for the planned extracapsular extraction, using a disposable or commercially available cystotome, several punctuations (60–80)
- Linear capsulotomy
- Capsulopuncture

Etiology

See "History" section above.

Treatment

After inflating the capsular bag with high-viscosity viscoelastic agents, a 1–2 mm relaxing capsulotomy is conducted at the center of the posterior capsule. To push the anterior vitreous face backward, 0.1 ml of the same agent is injected under posterior capsule. The resulting posterior capsule flap has to be teared outward while holding it with a forceps. Because of the nature of the

posterior capsule (thinner, more slippery, and elastic compared to the anterior capsule), a frequent and repeated regrasping of the capsular edge has been highly beneficial clinically.

The ideal size of this capsulorhexis should be approximately 4–5 mm.

A dye-enhanced posterior capsulorhexis may be adjuvant (0.1 ml of 0.1% trypan blue).

In case of pediatric surgery, the diameter of the posterior capsulorhexis is considered to be 1.0–1.5 mm smaller than the optic of the implanted intraocular lens.

Cross-References

- ▶ Can-Opener Technique
- ▶ Capsular Bag Opacification
- ▶ Cataract Surgery
- ▶ Nd:Yag-Capsulotomy
- ▶ Secondary Cataract

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Posterior Capsulotomy

- ▶ Posterior Capsulorhexis

Posterior Chamber

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Definition

Anatomical fluid-filled section of the eye which is defined between the back of the iris and the suspensory ligament of the lens as well as the ciliary processes. The posterior chamber is filled with aqueous humor which is produced in the ciliary processes and flows from the posterior chamber through the pupil aperture into the anterior chamber.

Cross-References

- ▶ Anterior Chamber
- ▶ Aqueous Humor
- ▶ Ciliary Body

Posterior Chamber Phakic Intraocular Lens

- ▶ Collamer Intraocular Lens
- ▶ PRL Phakic Intraocular Lens

Posterior Continuous Circular Capsulorhexis (PCCC)

- ▶ Posterior Capsulorhexis

Posterior Corneal Dystrophies

- ▶ Endothelial Degenerations

Posterior Corneal Mapping

- ▶ Computerized Corneal Topography

Posterior Crocodile Shagreen

► Corneal Dystrophies

Posterior Embryotoxon, Neurocristopathy

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Definition

Posterior embryotoxon is a prominent, anteriorly displaced Schwalbe's line that can extend 360° around the peripheral cornea or be isolated to a few clock hours, located most often, in the temporal aspect of the cornea. It can often be visualized on slit lamp exam, otherwise is seen gonioscopically.

Etiology

Dysgenesis of neural crest cells of the anterior chamber causes posterior embryotoxon. It can be isolated (i.e., considered normal) or be associated with a more extensive disease process such as Axenfeld-Rieger syndrome or Alagille's syndrome. Less commonly, it is seen in congenital glaucoma or iridocorneal endothelial syndrome. Histologically, it appears as a central core of collagen and ground substance covered by a layer of spindle shaped cells and basement membrane. In Axenfeld-Rieger syndrome, iris strands may extend to the posterior embryotoxon.

Occurrence

Posterior embryotoxon is present in 8–15% of normal individuals. It is most commonly seen in Axenfeld-Rieger syndrome, and seen in most, but not all, individuals with this disorder.

Classification

No classification system established.

Cross-References

► Axenfeld-Rieger Syndrome; Mesodermal Dysgenesis; Leukomas
► Schwalbe's Line

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Posterior Fossa Stare

► Collier's Sign

Posterior Inferior Cerebellar Artery Syndrome

► Wallenberg Syndrome

Posterior Ischemic Optic Neuropathy

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Synonyms

Arteritic PION (A-PION); Nonarteritic PION (NA-PION); Perioperative PION; Retrobulbar optic neuropathy; Surgical PION

Definition

The optic nerve is divided into two segments based clinically on the presence or absence of disk edema anterior or posterior to the lamina cribrosa. Posterior ischemic optic neuropathy (PION) is defined as acute ischemia of the posterior segment of optic nerve (retrobulbar optic neuropathy).

Etiology

PION can be divided into three main categories based on etiology: (1) arteritic PION (A-PION) is ischemia due to giant cell arteritis (GCA), (2) non-arteritic PION (NA-PION) is ischemia due to causes other than GCA, and (3) postsurgical PION. NA-PION is rare compared with typical NA anterior ischemic optic neuropathy (NAION); the ischemic event is thought to be multifactorial in nature and is associated with a variety of systemic diseases, including diabetes mellitus, arterial hypertension, arteriosclerosis, atherosclerosis, and arterial hypotension. These systemic diseases may be risk factors in the development of PION, as their prevalence is much higher in patients with PION versus the control population. In general, systemic diseases with vascular risk factors and defective autoregulation may predispose patients to the development of PION. The last type of PION is surgical PION (typically spine or cardiac surgery) with pathogenesis also likely to be multifactorial in nature. Major reported associations include duration of surgery, face-down positioning, prolonged arterial hypotension, prolonged general anesthesia, massive blood loss and anemia, hemodilution from large amounts of IV fluids, use of colloid versus crystalloid fluid replacement, use of the Wilson frame in spine surgery, and postsurgical orbital and periorbital edema. Surgical PION is thus associated with prolonged systemic surgical procedures most commonly after spine surgery or cardiac surgery but has also been reported in multiple types of surgery including orthopedic procedures, radical neck dissection, venous graft procedures in extremities, and hip surgeries.

Clinical Presentation

The clinical presentation varies depending on the etiology of PION. Those with A-PION and NA-PION usually present with painless and acute visual loss in one or both eyes. Patients

with GCA typically have other constitutional symptoms including headache, scalp tenderness, jaw claudication, fever, or polymyalgia rheumatica. Patients with PION may discover visual loss upon waking up in the morning, and others may experience more acute and then progressive symptoms during waking hours. Patients with surgical PION often notice unilateral or bilateral visual loss or blindness immediately upon awakening postoperatively, but some patients with surgical PION do not report their visual complaints until later. Visual acuity and visual field defects are variable in PION. However, the most common visual field defects are nerve fiber layer type. Unilateral or asymmetric bilateral PION will likely present with a relative afferent pupillary defect, but the remainder of the ocular exam is typically normal. Generally within 6–8 weeks, disk pallor will develop in the affected eye(s).

Diagnosis of PION

PION is a diagnosis of exclusion as other forms of retrobulbar optic neuropathy can mimic the clinical presentation. A combination of the following findings are suggestive of PION: (1) sudden and acute onset of visual deterioration that may be accompanied by deterioration of central visual acuity, (2) visual field defect in the affected eye, (3) relative afferent pupillary defect in the affected eye, (4) initially normal optic disk and fundus on both ophthalmoscopy and perhaps concomitant fluorescein fundus angiography, (5) no other abnormalities that may explain the visual loss, and (6) optic disk pallor that develops within 6–8 weeks. However, the diagnosis of surgical PION can be based on drastic visual loss noted upon patient awaking from a major surgical procedure.

Differential Diagnosis

Nonarteritic AION, macular and retinal lesions, retrobulbar optic neuritis, compressive optic neuropathy, neurological lesions.

Prophylaxis

There is no prophylaxis beyond controlling vasculopathic risk factors for NPION, but some measures to reduce the risk of postsurgical PION have been proposed including monitoring for and avoiding excessive arterial hypotension or hemodilution, attention to fluid management (colloid versus crystalloid fluid replacement), avoiding direct pressure on the orbit, shortening the duration of surgery to a minimum and/or staging the procedure if necessary, avoiding vasoconstrictors, transfusion for anemia, and prone positioning with the head at the level of the heart. Unfortunately, no single countermeasure has proven to be effective as surgical PION which is likely multifactorial has no proven single proximate cause. In addition, treatment of one risk factor (e.g., hypotension) might worsen another risk factor (e.g., increased bleeding or surgical time). In terms of NA-PION, since it is associated with several systemic risk factors, reducing as many risk factors as possible may reduce the risk of eye involvement.

Therapy

Management of PION depends upon the etiology.

Prognosis

Visual prognosis in PION is variable. In general steroid therapy is given to GCA PION patients to prevent fellow eye involvement. Most patients with surgical PION do not recover their vision and the role of steroids is unproven. NA-PION has a variable rate of spontaneous recovery that may be better than GCA-related PION or surgical PION.

Epidemiology

PION is much less common than AION, and its true incidence is difficult to assess considering it is a diagnosis of exclusion. The exact incidence of

surgical PION is also unknown, but they are most frequently reported after cardiac and spinal surgeries.

Cross-References

- ▶ Arteritic Anterior Ischemic Optic Neuropathy
- ▶ Giant Cell Arteritis
- ▶ Nonarteritic Anterior Ischemic Optic Neuropathy

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Posterior Lamellar Keratoplasty

- ▶ Deep Lamellar Endothelial Keratoplasty (DLEK)

Posterior Lenticonus

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Definition

Posterior lenticonus is a unilateral or bilateral thinning and posterior bowing of the posterior capsule of the crystalline lens.

Etiology

Sporadic cases of posterior lenticonus occur. In many cases, posterior lenticonus is inherited (x-linked, autosomal dominant trait or autosomal recessive inheritance). Posterior lenticonus has been associated with microcornea, hyperglycinuria, Duane's syndrome, Alport syndrome, and anterior lentiplanus.

Clinical Presentation

In a slit-lamp examination, a spheroidal or conical protuberance affecting the posterior lens surface can be observed. Opacification of the adjacent lens cortex may occur, and posterior lenticonus may manifest as a high degree of astigmatism.

Diagnostics

Posterior lenticonus can be diagnosed in a slit-lamp examination or with ultrasound biomicroscopy.

Differential Diagnosis

Posterior subcapsular cataract.

Therapy

Mild cases may be observed. More severe cases with progressive opacity of the lens lamellae or risk of amblyopia due to high astigmatism may require cataract surgery with a posterior capsulorhexis during the first months of life.

Prognosis

The prognosis is usually good if no amblyopia has developed.

Epidemiology

Posterior lenticonus is a rare disease.

Cross-References

- ▶ Astigmatism
- ▶ Cataract, Causes and Treatment
- ▶ Microcornea
- ▶ Nutritional Amblyopia

Further Reading

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Posterior Optic Buttonholing

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Synonyms

POBH

Definition

Surgical technique during phacoemulsification for reduction of posterior capsule opacification.

Epidemiology

No epidemiologic data available for this topic.

History

In 2006, Menapace introduced this technique to preserve full capsular transparency and to evaluate it as a potential routine alternative to standard in-the-bag implantations of sharp-edged optic intraocular lenses. It has also been used in cataract surgery with children to prevent aftercataract.

Clinical Features

See Treatment section below.

Tests

Thorough examination of the anterior segment with the slit-lamp gonioscopy, measurement of uncorrected and best spectacle-corrected visual acuity and intraocular pressure, and biometry are mandatory to maintain best possible postoperative results.

Differential Diagnosis

Other surgical techniques for reducing posterior capsule opacification ARE:

– Anterior capsulorhexis fixation

Etiology

See History section.

Treatment

After topical anesthesia, standard anterior capsulorhexis and phacoemulsification are performed. Remaining opacifications of the anterior and posterior capsule are polished bimanually. Injection of viscoelastic is necessary to separate the capsule leafs from each other and to lift the posterior capsule from the vitreous surface.

After implantation of the intraocular lens and enclavation of the haptic in the chamber fornix, slight pressure is performed on the optic at 6 o'clock until it moves behind the posterior capsule. The same maneuver is done at 12 o'clock of the optic and the viscoelastic is removed. Finally, when observing the intraocular lens, the anterior rhexis shows a round form, whereas the posterior rhexis is oval.

Cross-References

- ▶ After Cataract
- ▶ Phacoemulsification and Posterior Chamber Intraocular Lens (IOL) Implantation
- ▶ Posterior Capsulorhexis

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Posterior Polar Cataract

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Definition

A posterior polar cataract is a congenital or infantile subcapsular cortical opacification at the posterior pole of the crystalline lens.

Etiology

The opacification consists of abnormally developed lens fibers attaches to the posterior capsule. Posterior polar cataract occurs sporadically, but there is also an autosomal dominant familiar form which is in most cases bilateral. The sporadic form is sometimes associated with other abnormalities such as remnants of the tunica vasculosa lentis, lenticonus. or lentiglobus.

Clinical Presentation

As in other forms of cataract the disease causes variable degrees of decrease in visual acuity and contrast sensitivity as well as symptoms of glare depending on the size of the lesion. Because of the proximity to the nodal point of the eye posterior polar cataracts cause more visual impairment than anterior polar cataracts. Especially, unilateral cases can cause amblyopia.

Diagnostics

The posterior polar cataract is seen in slit-lamp microscopy as a central subcapsular opacification at the posterior lens pole in an otherwise clear lens.

Differential Diagnosis

Similar lesions may occur due to posterior capsule trauma, e.g., due to previous vitreoretinal surgery.

Prophylaxis

There is no known prophylaxis against this condition.

Therapy

As in other forms of cataract, the therapy is surgical. Because of a high incidence of increased capsular fragility or preformed posterior capsular openings cataract surgery in eyes with posterior polar cataract has a higher than average risk of posterior capsule rupture and care must be taken to minimize stress on the posterior capsule. In 20% of cases, a primary posterior capsule defect has been reported.

Prognosis

Usually, the condition is stable and does not progress. However, a progressive form which usually becomes symptomatic between 30 and 50 years of age has been described.

Epidemiology

It is generally agreed that posterior polar cataract is a rare disease. No publications about its incidence and prevalence are available.

Cross-References

- ▶ Capsular Bag
- ▶ Cataract, Causes and Treatment
- ▶ Nutritional Amblyopia
- ▶ Phacoemulsification and Posterior Chamber Intraocular Lens (IOL) Implantation

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Posterior Polymorphous Corneal Dystrophy

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Synonyms

Posterior polymorphous dystrophy (PPMD); Schlichting dystrophy

Definition

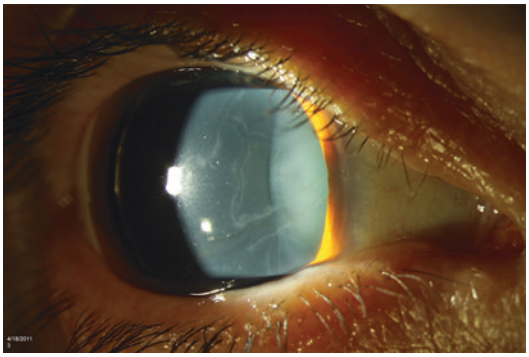
Endothelial corneal dystrophy.

Etiology

Posterior polymorphous corneal dystrophy (PPCD) is an autosomal dominantly inherited corneal dystrophy. Three genetic loci – PPCD 1 through 3 – have been isolated to chromosomes 20, 1, and 10, respectively. Mutations in *COL8A2* (collagen type VIII alpha 2) and *ZEB1* (two-handed zinc-finger homeodomain transcription factor 8) are responsible for PPCD 2 and PPCD 3. The gene implicated for PPCD 1 has not been isolated.

Clinical Presentation

The onset of PPCD is in early childhood. Patients often present with asymmetric, deep corneal lesions of various morphologies including nodular, vesicular, and blister-like lesions. Patients can also present with deep stromal broadbands with scalloped edges have been termed "railroad tracks" (Fig. 1a, b). Geographic-shaped lesions at the level of Descemet's membrane are often present. Stromal and epithelial edema can be variably present



Posterior Polymorphous Corneal Dystrophy, Fig. 1 Posterior polymorphous dystrophy showing deep stromal bands with scalloped edges ("Railroad tracks"). (**a**) Posterior polymorphous corneal dystrophy, displaying deep stromal bands with scalloped edges ("railroad tracks"). (**b**) Posterior polymorphous corneal dystrophy, retro-illumination view highlights deep stromal bands with scalloped edges ("railroad tracks")

due to endothelial decompensation. Peripheral iridocorneal adhesions can also be present. In about 15% of cases, intraocular pressure is elevated.

Diagnosis

The diagnosis of PPCD is often made on the basis of the clinical exam. Biopsy of corneal tissue can reveal the distinctive light microscopic finding of PPCD: the appearance of abnormal, multilayered endothelial cells that resemble epithelial cells or fibroblasts. Light microscopy can also reveal thickened Descemet's membrane with multiple layers of collagen on its posterior surface manifesting focal fusiform or nodular excrescences. Confocal microscopy reveals polymegathism of the endothelium. Vesicular lesions in PPCD appear as doughnut-like areas (rounded dark areas with some detail in the middle) on confocal microscopy.

Differential Diagnosis

Differential diagnosis includes Fuchs endothelial corneal dystrophy and congenital hereditary endothelial dystrophy 1.

Therapy

While most remain asymptomatic, some patients can develop stromal edema due to endothelial decompensation. Mild edema can be managed with sodium chloride drops and ointment. Advanced edema can be managed with either endothelial or penetrating keratoplasty. PPCD can recur in a graft. Concomitant glaucoma must be managed if present.

Prognosis

Patients are often asymptomatic. Endothelial signs of PPCD often remain unchanged over years. Rarely there is slow progression of these lesions leading to endothelial decompensation. Congenital corneal clouding is extremely rare.

Epidemiology

Rare

Cross-References

- ▶ Congenital Hereditary Endothelial Dystrophy
- ▶ Fuchs' Endothelial Corneal Dystrophy
- ▶ Posterior Corneal Dystrophies

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Posterior Polymorphous Dystrophy (PPMD)

- ▶ Corneal Dystrophies
- ▶ Posterior Polymorphous Corneal Dystrophy

Posterior Uveal Bleeding Syndrome (PUBS)

▶ Polypoidal Choroidal Vasculopathy

Posterior Vitreous Detachment

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Definition

Posterior vitreous detachment (PVD) is the most frequent and most important change of the vitreous, which is defined as the separation of posterior hyaloid membrane from the internal limiting membrane (ILM). Although PVD naturally resulted from aging and usually harmless, PVD can be the provoking event for numerous vitreoretinal pathologies. It has been shown that up to 24% of symptomatic PVD gives rise to retinal complications (Yonemoto et al. 1994; Hikichi and Trempe 1994; Chuo et al. 2006). According to the existence of adhesion at the vitreoretinal interface and its sequelae, PVD can be divided into complete or partial and innocuous or anomalous PVD.

Epidemiology

Studies have shown the incidence of PVD is 66% between the ages of 66 and 86 years and 53% after 50 years (Favre and Goldmann 1956). The average age of onset of PVD is approximately 61 years old (Yonemoto et al. 1994). In cases suffered from myopia, retinal vascular disorders, trauma, and retinitis pigmentosa, the onset may occur at a younger age (less than 40 years old) (Yonemoto et al. 1994; Sebag 1993; Akiba 1993; Hikichi et al. 1995; Morita et al. 1995). Female gender is one of the risk factors of development of PVD. The average age of onset for females has been shown to be statistically significantly earlier than males which have been attributed to postmenopausal loss of estrogen. The development of new technics, including clinical examination, ultrasonography, monochromatic photography, and optical coherence tomography, helps to improve the assessment of PVD.

Etiology

The vitreous, a transparent, avascular gel, contains 98% of water and 2% of low molecular weight solutes and macromolecules. The major molecular constituents are hyaluronic acid (HA), collagen, a wide range of soluble proteins, and some other components, including heparin sulfate, chondroitin sulfate, and opticin. These molecules are the main ingredients that maintain the gel-like and transparent appearance of the vitreous. However, under aged or pathologic condition, the architecture features of the vitreous experience dramatic changes as degeneration causes syneresis, cavity formation, and collapse of the vitreous gel.

Liquefaction and vitreoretinal interface weakening are the most important processes of vitreous aging that occur in parallel. Age-related liquefaction is called "synchysis senilis." However, the first appearance of liquid vitreous was observed at the age of 4 years; after age 40 years, there is a significant decrease in the gel volume and a concurrent increase in the liquid volume of the vitreous, and by the age of 80–90 years, more than half the vitreous is liquid (Foos and Wheeler 1982; Williamson and Williamson 2013). Actually, there is no consensus on the explicit reason of gel liquefaction. Myopia is a notable cause of vitreous liquefaction in younger individuals. Yonemoto et al. demonstrated that 0.91 years could be subtracted from the average age of PVD for each diopter of myopic refractive error (Yonemoto et al. 1994). Beside increase of liquid in the vitreous, the collagen malformation is also the etiology of liquefaction. Inherited collagen metabolic disorders such as Marfan, Ehlers-Danlos, Stickler, and Knobloch syndromes are

usually accompanied by advanced vitreous liquefaction. Along with the advancing vitreous liquefaction, cavities of liquid vitreous called lacunae arise within the gel-like architecture.

In the context of weakening of vitreoretinal adherence, chondroitin sulfate, opticin, and/or other components are lost or altered and at the same time will promote the aggregation of vitreous collagen fibrils into visible fibers called "aggregation of the vitreous," which eventually leads to the collapse of the vitreous body. Complete PVD dissects completely the posterior vitreous cortex and the inner limiting membrane of the retina; it usually has no abnormal adhesion at the vitreoretinal interface. It's clinically innocuous and has dominance in the elderly. When the vitreoretinal dehiscence is insufficient, the liquefied vitreous cannot pull away thoroughly. Some parts of the vitreous cortex at the posterior vitreoretinal interface will be detached, which is called partial PVD. One special situation is called vitreoschisis (VS), which means there is a split in the posterior vitreous cortex. Any factor that breaks the balance between the degree of gel liquefaction and the vitreoretinal adhesion can lead to PVD. Those factors can be congenital like Marfan, Ehlers-Danlos, and Stickler syndromes or secondary from systemic diseases such as proliferative diabetic vitreoretinopathy and diabetic macular edema. Likewise, numerous eye complaints such as trauma, inflammation, and myopia disturb the homeostasis of vitreous body and lead to PVD.

Posterior Vitreous Detachment, Table 1 Complications of posterior vitreous attachment

Origins	Retinal complications
Age-related posterior vitreous detachment	Retinal tears
	Rhegmatogenous retinal detachment
	Macular epiretinal membrane
	Vitreomacular traction syndrome
	Macular hole
	Vitreous hemorrhage
Pathological vitreous separation	Diabetic tractional retinal detachment
	Posterior uveitis
	Trauma

Clinical Presentation

Symptoms

Floaters

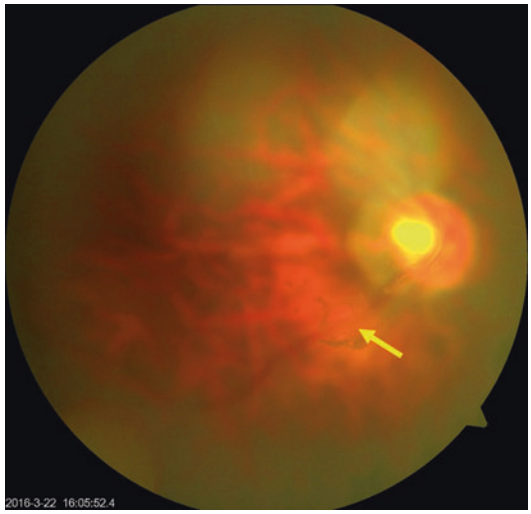
Though PVD is usually asymptomatic or without pathological complications, the most common symptom arising from PVD is floaters. Floaters can be resulted from the shadows casted by Weiss ring, intravitreal blood, or condensed vitreous fibers. A Weiss ring, a small ring of tissue in front of the optic disk, is the gliotic tissue avulsed from the disk margin during PVD, which indicates the development of posterior vitreous detachment. The patients with floaters often complain a cobweb, spider, veils, a ring, and a spot or multiple spots that move with the eye movements.

Flashes

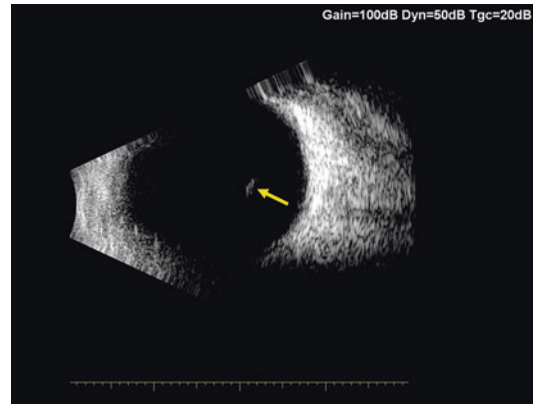
Photopsia or "lightning flashes," another distinguished clinical symptom of PVD, are described as "a light from non-photic stimulation or a flash-like appearance of the lights," which lasts typically a second at a time, usually vertical, and almost always in the temporal periphery of their visual field (Williamson and Williamson 2013). Their exact pathogenesis is obscure but thought to be resulted from either traction or impact exerted by the vitreous onto the retina. The traction retina existing upon the vitreoretinal interface during PVD can lead to sight-threatening complications (Table 1), such as retinal breaks, retinal detachments, and hemorrhages called anomalous PVD. Patients who experience symptomatic PVD have a 10% risk of retinal tears, which should be kept in mind by every health practitioner. Flashes from PVD may diminish in a few months with the relief of traction but may not vanish completely.

Signs

Complete PVD can be diagnosed by examining the eye with a 90-diopter lens as the detection of a Weiss ring (Fig. 1). Although the ring is often incomplete and absent in 13% of PVD (Akiba



Posterior Vitreous Detachment, Fig. 1 A Weiss ring (*yellow arrow*) in the posterior vitreous cortex following PVD in front of the optic disk (color fundus image) (Color fundus image was taken from a PVD patient and provide by Dr. Jacey Hongjie Ma.)



Posterior Vitreous Detachment, Fig. 2 Ultrasound B-scan of a posterior vitreous detachment showing a Weiss ring (*yellow arrow*) (Ultrasound B-scan was taken from a PVD patient and provide by Dr. Jacey Hongjie Ma.)

et al. 2001; Kakehashi et al. 1998), the posterior hyaloid membrane can be seen in these patients and an optically clear space, behind the membrane, suggesting the absent of the vitreous. Though in complete PVD, the vitreoretinal adhesion at the peripheral part of the retina, around the ora serrata, persistently exists. This adhesion is the reason of the formation of retinal tear usually within the first 6 weeks after onset of symptoms. Retinal tears are complicated in 10% of symptomatic PVD (van Overdam et al. 2001).

Another important sign of PVD, named Shafer's sign, can be observed as some pigment granules in anterior vitreous, owning to the retinal pigment epithelial (RPE) cells released through the retinal tear. The existence of Shafer's sign indicates the presence of a retinal tear from PVD (Tanner et al. 2000; Dayan et al. 1996; Byer 1994; Brod et al. 1991).

Besides Shafer's sign, vitreous hemorrhage should also raise suspicion of pathology. Though red blood cells are more difficult to be seen than RPE cells in the vitreous, 50% of patients with RBCs in the vitreous are having retinal tears (Williamson and Williamson 2013). Once RBCs are indicated, retinal tear should be examined carefully. If vitreous hemorrhage is severe and the retina is hard to be visualized, the B-scan ultrasonography should be taken, and a pars plana vitrectomy (PPV) may be chosen to remove the hemorrhage and fix the break when necessary.

Diagnosis

The diagnosis is mainly made after a careful clinical examination with a 90-diopter lens, and different imaging modalities aid with better performance in diagnosing, categorizing, and assessing the insult. B-scan ultrasonography is an established and helpful method to detect and characterize PVD (Fig. 2) and other possible complications such as vitreous hemorrhage, vitreous macular traction, and retinal detachment, which can be easily imaged by B-scan ultrasound when the posterior vitreous cortex is separated from the retina.

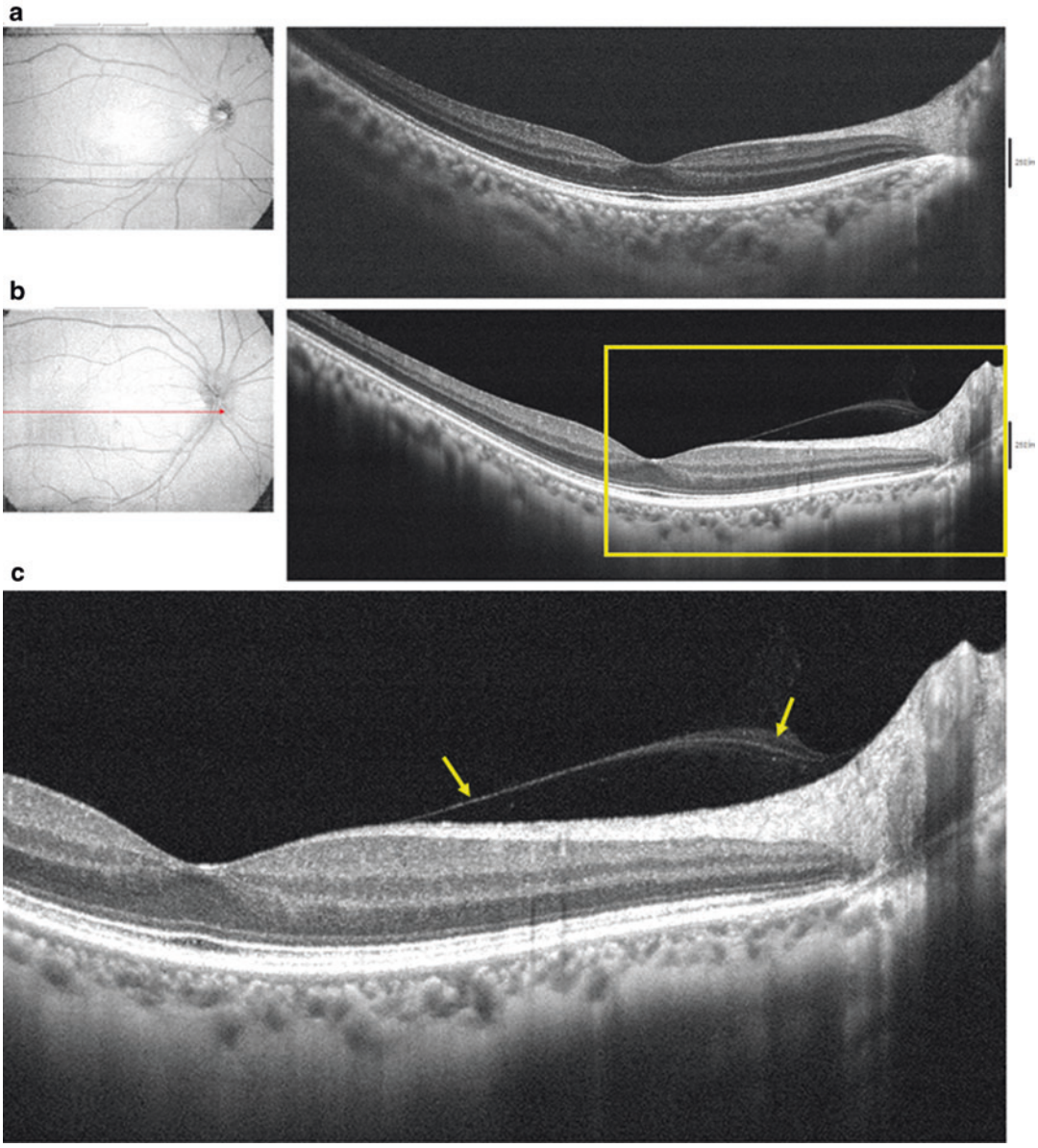
Newly developed optical coherence tomography technologies, such as spectral domain OCT (SD-OCT) and swept source OCT (SS-OCT), provide a detailed delineation of the posterior vitreous cortex, the inner limiting membrane (ILM), and the contour of macular and optic nerve (Fig. 3a), which often demonstrates a hyper-reflective line completely separating or partially adhering to the neurosensory retina from the vitreous (Fig. 3b, c).

Differential Diagnosis

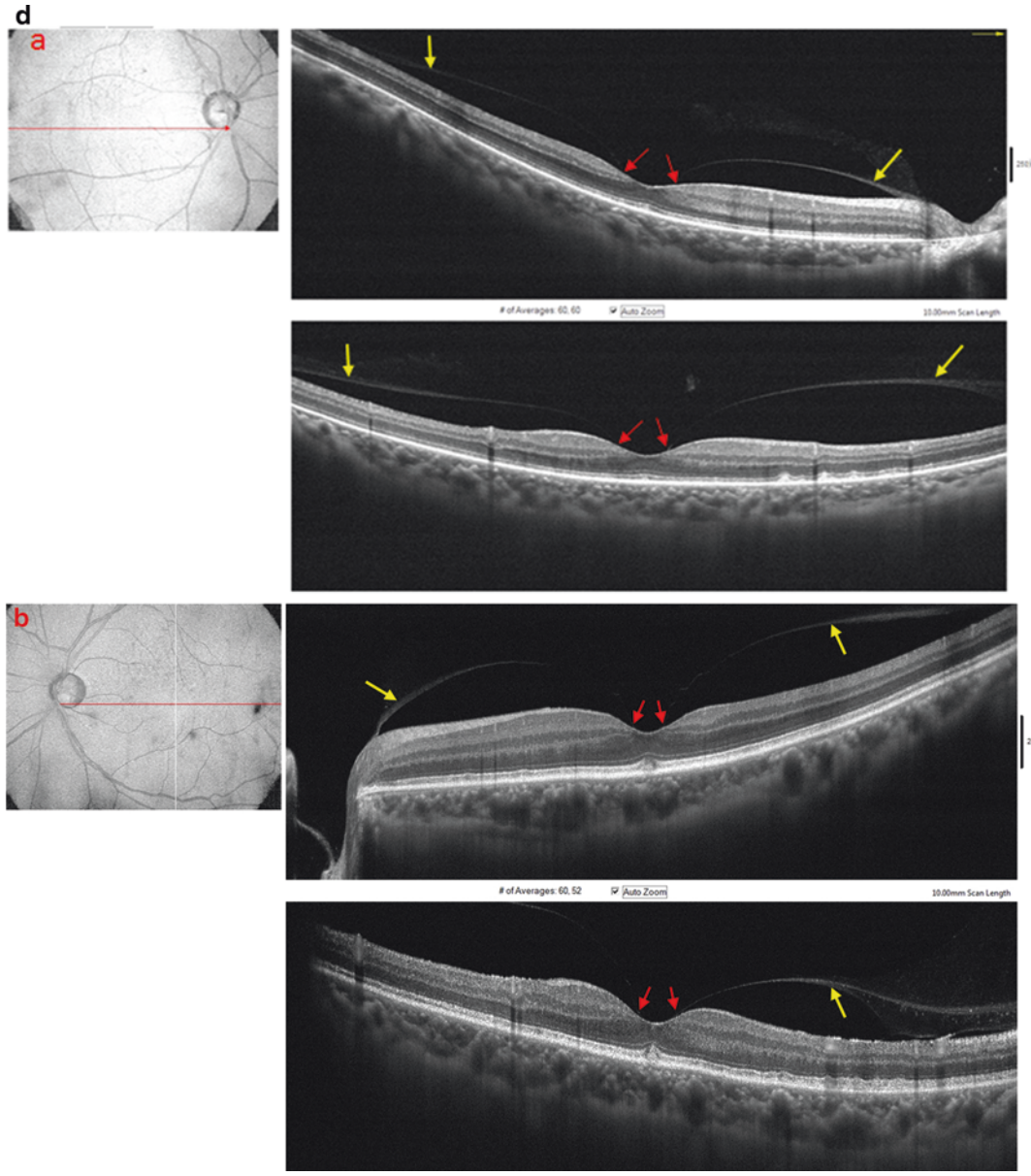
PVD should be discriminated from those diseases such as vitreous opacity, retinal detachment, zigzag lights of migraine, and flickering stars associated with occipital ischemia which have similar symptoms (floaters and lighting flashes). With the help of imaging modality aids, it can be easily discriminated.

Prophylaxis

Since the high incidence of retinal tears and macular disorders in symptomatic PVD, called anomalous PVD, may develop into sight-threatening diseases, such as rhegmatogenous retinal detachment, macular pucker, and macular hole, it should be taken seriously and checked intensively. The main prevention procedure is to examine the



Posterior Vitreous Detachment, Fig. 3 (continued)



Posterior Vitreous Detachment, Fig. 3 (**a**) SD-OCT image is showing normal interface between the vitreous and retina without PVD; (**b**) partial separation of the vitreous from internal limiting membrane. (**c**) Enlarge image of the yellow frame in (**b**) is showing the separation of the vitreous from internal limiting membrane (*yellow arrows*). (**d**) OCT images of a patient suffering PVD in both eyes (**a** right eye, **b** left eye). Posterior vitreous was separated from the retina (*yellow arrows*) except the macular fovea (*red arrows*) (SD-OCT images were provide by Dr. Jacey Hongjie Ma.)

complications of anomalous PVD, carefully, timely, and follow up regularly with a 90-D lens through a dilated pupil, especially in the cases with higher risks such as proliferative diabetic retinopathy, myopia.

Therapy

Though complete PVD, exempt from retinal tears or macular disorder, is clinically innocuous, routinely follow-up is recommended. In the cases

with visual disturbance caused by floaters, it can receive modern vitreolysis, also known as floater laser treatment. Vitreolysis is a noninvasive, pain-free procedure that can eliminate the opacity vitreous fibers or Weiss ring by YAG laser.

Anomalous PVD is usually accompanied by various complications, including retinal tears, retinal detachment, macular disorders, and the underlying diseases; therefore, further attention and appropriate treatment should be given when confronting those diseases.

Prognosis

For complete PVD which is usually caused by aging and is clinically innocuous, the prognosis is benign, while for anomalous PVD, visual acuity prognosis is often according to the extent of the complication and relies on the timely and appropriate intervention.

Cross-References

- ▶ Diabetic Retinopathy
- ▶ Optical Coherence Tomography
- ▶ Retinal Detachment
- ▶ Retinal Tears

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Postherpetic Neuralgia

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Synonyms

Nerve pain; Shingles

Definition

Postherpetic neuralgia (PHN) refers to pain, as well as associated itching and irritation, following acute herpes zoster infection. Reactivation of latent varicella zoster virus, which lies dormant in sensory ganglia, is the cause of herpes zoster.

This reactivation happens in about 30% of people over a lifetime. Of those with reactivation, a significant minority – roughly 10–20% – suffers from PHN. Resultant viral nerve damage, to both central and peripheral nervous systems, is thought to be the cause of PHN. More specifically, the generation of spontaneous neuronal discharges coupled with decreased activation threshold produces pain signals out of proportion to common stimuli. Symptoms localize to the skin and nerves affected by the herpes zoster rash. These can include burning, aching, or electric-shock-like pain. A spectrum of presentation is also common, ranging from mild dysesthesia to excruciating allodynia. The ophthalmic division of the trigeminal nerve is commonly involved. Other common areas of involvement are the thoracic, cervical, and lumbosacral dermatomes.

A precise definition of PHN is not agreed upon in the literature. In some clinical studies, a diagnosis of PHN is made 3 months after resolution of skin rash though other studies cite 120 days as the defining criterion. In practice, this definition is applied less conservatively and can be anywhere from 1 to 4 months after resolution of zoster. Additionally, it should also be noted that PHN can occur in the absence of rash (zoster sine herpete), making diagnosis even more difficult in some cases. At 1 month after the skin rash resolves, roughly 10% of patients have PHN.

Risk factors include increasing age, severe pain with initial infection, immunosuppression, and severe prodrome. Patients greater than 80 years of age carry a 35% risk of developing PHN as compared to a 20% risk for patients over the age of 50. PHN in those less than 50 years of age is rare – about 2%.

Due to the complex nature of this condition and an incomplete understanding of its pathophysiology, there are a wide variety of treatments that are available. First-line agents that have been shown to be effective include GABA agents and tricyclic antidepressants. Topical preparations such as 5% lidocaine are also reported to ease PHN. Furthermore, there are several other classes of drugs, like serotonin-norepinephrine uptake inhibitors and antiepileptic agents, which are the focus of investigation today. It is also interesting to note that, if given in the first 72 h of rash development, both antivirals and amitriptyline have been shown to decrease the intensity and duration of PHN probably secondary to the neuroprotective benefits they confer. Studies have shown that PHN has significant detrimental effects on quality of life including increases in insomnia, depression, fatigue, and cognitive impairment. Significant economic impact is another sequela of PHN given its effects on upwards of 2,000 individuals per year in the United States. A vaccine for herpes zoster is currently available and has been effective in reducing the burden of herpes zoster and in turn PHN. Fortunately, though no cure exists, symptoms associated with PHN often fade over time.

Cross-References

- ▶ Herpes Zoster
- ▶ Herpes Zoster Ophthalmicus

Postseptal Incision

- ▶ Transseptal Route, for Anterior Orbitotomy

Potential Acuity Meter

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Purpose

The marco Guyten-Minkowski potential acuity meter (PAM) projects an eye chart directly on

the retina and bypasses the cataract. This allows the examiner to test for visual acuity without interference from the cloudy lens (Minkowski et al. 1983).

Principle

Mounted on a slit lamp, the PAM projects a Snellen visual acuity chart into the eye via a narrow beam of light converging to a minute aerial aperture of 0.1 mm in diameter. The examiner aims the narrow beam through "windows" in the cataract, avoiding blockage or scattering of the light that would otherwise occur. Without diffraction from the edges of the aperture or loss of illumination, this allows for determination of retinal acuity (Minkowski et al. 1983).

The potential acuity meter (PAM) must not be mixed up with a retinometer (Visometer), which uses interference for projection of sinusoidal patterns o the retina, while the PAM projects an image of, e.g., a Snellen letter or number chart on the retina (Faulkner 1983; Reid et al. 2007). Current models of both devices, however, seem to provide the same quality of results, if used properly (Reid et al. 2007).

Indication

The PAM is used for fast estimation of potential postoperative visual acuity, when classical visual acuity testing due to a blurred lens (e.g., in cataract) is not possible. It can furthermore be used for fast visual acuity screening without refraction in vitreoretinal, retinal vascular, or neurophthalmic patients as well as in patients with large and/or irregular refractive errors.

Contraindication

Some limitations that may cause more tedious testing or even may make testing impossible are: poor pupillary dilation, dense media (finger counting), poor patient posture, communications problem, alphabet illiteracy, nystagmus, senility, or fatigue.

Advantage/Disadvantage

The major advantage of the PAM is the option to measure visual acuity in dense, though not intransparent, optical media. However, optical distorsions caused by, e.g., irregular corneal astigmatism (keratoconus) remain undetected, if no additional corneal diagnostic is performed. PAM measurements of visual acuity should thus always be performed in combination with slit-lamp imaging and corneal topography to exclude other causes of potential postoperative visual acuity impairment.

Cross-References

- ▶ Cataract, Causes and Treatment
- ▶ ETDRS Visual Acuity Chart
- ▶ Retina, Structure of

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Pox

- ▶ Syphilis: Overview

Precorneal Tear Film

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Synonyms

Lacus lacrimalis; Tear lake; Tear meniscus

(These terms refer specifically to the collection of tears at the lower lid – globe interface.)

Definition

Layer of tears overlying the cornea and ocular surface.

Structure

The tear film was traditionally conceptualized as having three discrete layers: a mucin layer, an aqueous layer, and an outer lipid layer. It has subsequently become clear that the constituents of the tear film interact more dynamically, but it is still useful to discuss the structure and function of these layers individually (Colby 2006).

The innermost layer abutting the cornea is formed of high molecular weight glycoproteins known as mucins. Some of these are bound to the outer microvilli-laden surface of the epithelial cells. The secreted mucins, which also interact with the aqueous phase of the tear film, easily slide over their membrane-bound counterparts due to electrostatic repulsion. The majority of mucins are produced and secreted by conjunctival goblet cells, but the lacrimal gland and squamous epithelial cells may generate some as well. The aqueous layer of the tear film contains water, electrolytes, proteins such as albumin, growth factors, immunoglobulins, and antimicrobial molecules such as lysozyme and lactoferrin. Lipid secretions from the meibomian glands, as well as the glands of Zeiss and Moll, constitute the outer oily layer of the tear film.

Function

The integrity of the tear film is critical to creating a clear refractive surface as well as to protecting the cornea from dessication, breakdown, and infection. It is constantly replenished, and the dynamic flow from the lacrimal gland to the drainage system serves to clear foreign materials, inflammatory mediators, and microbes.

Mucins facilitate interactions between hydrophobic cell membrane components and the aqueous phase, as well as help to bind and clear debris. Electrolytes in the tear film serve to buffer the pH and to create a favorable environment for the epithelial cells. Growth factors and cytokines are critical to promoting epithelial cell turnover and migration. Immunoglobulins and other antimicrobial molecules are an important component of the host defenses. The lipid layer protects against rapid evaporation of the tear film.

Clinical Relevance

The tear film is adversely affected in a variety of dry eye conditions, which are broadly categorized as either aqueous tear deficiency (ATD) or evaporative tear deficiency (ETD), although the two frequently overlap (Peng et al. 2014). Aqueous tear deficiency is further subdivided into Sjögren's- and non-Sjögren's-related groups.

Schirmer tests have traditionally been used to measure aqueous tear production and can be performed with our without anesthesia. Vital dyes such as fluorescein, lissamine green, and rose bengal are often used to assess the tear film and ocular surface. In addition to highlighting epithelial defects or areas of punctate keratopathy, fluorescein is useful for assessing tear breakup time (TBUT) and for approximating the height of the tear meniscus (Chen et al. 2010).

More recently, techniques such as tear osmolarity measurement, interferometry, and high-resolution optical coherence tomography (OCT) have gained popularity for quantitative assessments of the tear film (Hosaka et al. 2011; Werkmeister et al. 2013).

Cross-References

- ▶ Dry Eye
- ▶ Goblet Cells, Mucin Tear Secretion by
- ▶ Meibomian Gland Dysfunction
- ▶ Schirmer Tests
- ▶ Tear Breakup Time
- ▶ Tearing (Epiphora)

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Predescemet Deep Anterior Lamellar Keratoplasty

- ▶ Deep Anterior Lamellar Keratoplasty (DALK)

Preperiosteal Midface Lift

- ▶ Cheek Elevation, in Eyelid Repair

Preretinal Macular Fibrosis

- ▶ Cellophane Maculopathy

Preretinal Macular Gliosis

- ▶ Cellophane Maculopathy

Preretinal Vitreous Membranes

- ▶ Cellophane Maculopathy

Presbyopia

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Definition

Presbyopia is the loss of the accommodating ability of the eye that occurs with advancing age.

Course

The loss of accommodative ability begins at a young age. At the age of 35 years already two thirds of the accommodative amplitude has been lost. At 60 years of age, the ability for accommodative change in the dioptric power of the eye has completely disappeared (Duane 1912).

Possible Causes

Accommodation is effected by a change in shape of the crystalline lens. Therefore, it is conceivable that presbyopia is caused by hardening of the lens substance. This means that with advancing age the

ciliary muscle action occurring with an accommodative effort is not accompanied by the corresponding changes in lens power. Experimental studies in vitro found that the ability of the human crystalline lens to change its shape under the influence of mechanical stretching diminishes continuously with advancing age up to the age of 60 years. After that no change occurs at all (Glasser and Campbell 1998). Corresponding to these results are other studies showing evidence for progressive hardening of the lens substance with age (Weeber et al. 2007). The lens capsule, on the other hand seems to keep most of its elasticity even into advanced age. The insertion of the anterior zonule near the lens equator shifts anteriorly with advancing age while the distance to their origin at the ciliary body remains constant. This could in connection with the increasing thickness of the lens play a role in the development of presbyopia. The loss of elasticity of the posterior tendons of the ciliary muscle as well as the age-related degeneration of muscle and nerve fibers with consecutive changes in ciliary muscle configuration could as well potentially contribute to the age-related loss of accommodation. Several studies show a decrease of the ciliary muscle ring diameter and the movement of the muscle with accommodation. There are also existing hypotheses that the vitreous body has a stabilizing effect on the lens during accommodation and that the age-related liquefaction of the vitreous is a contributing factor to the loss of accommodation.

Lenticular and ciliary origins of presbyopia are not mutually exclusive. Most probably presbyopia has multifactorial causes, but so far the hardening of the lens substance seems to play the most important role among the factors responsible for the age-related loss of accommodation (Glasser et al. 2003).

Cross-References

- ▶ Accommodation, Cataract
- ▶ Cataract, Causes and Treatment
- ▶ Ciliary Muscle
- ▶ Lens Capsule

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Preseptal Fat

▶ Sub-brow Fat Pads

Presumed Tuberculous Retinal Periphlebitis

▶ Eales' Disease

Pretectal Syndrome

▶ Dorsal Midbrain (Parinaud) Syndrome, Convergence-Retraction Nystagmus, Eyelid Retraction

Primary Acquired Melanosis

▶ Pigmented Lesions of the Conjunctiva

Primary Angle Closure

▶ Acute Angle Closure

Primary Angle Closure and Angle Closure Glaucoma

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Synonyms

Narrow angle glaucoma; Narrow drainage angle

Definition

Primary angle closure is defined by iridotrabecular contact in eyes with an anatomic predisposition but no further pathology causing narrow angle or peripheral anterior synechiae (PAS).

In primary angle closure, elevated intraocular pressure (IOP) or PAS are present, but no evidence for glaucomatous optic neuropathy (GON) is seen. Features indicating that trabecular obstruction by the peripheral iris has occurred, as well as symptoms suggestive of episodes of primary ▶ acute angle closure, may be found.

The term primary ▶ angle closure glaucoma is used if GON is present, although elevation of IOP or PAS may be absent at the time of initial examination.

Primary ▶ acute angle closure is defined by an excessive rise of IOP with acute symptoms, whereas intermittent primary angle closure is a condition in which ▶ angle closure occurs with abortive symptomatic.

Chronic primary angle closure is defined as synechial closure (▶ angle closure), usually without typical clinical symptoms, unless severe GON is present.

Etiology

Relative pupillary block is considered to be the most common underlying cause of primary angle closure and angle closure glaucoma. Due to an anatomic predisposition, trans-pupillary aqueous flow resistance is increased, followed by forward bowing of the peripheral iris and iridotrabecular contact with occlusion of the anterior chamber angle. Lens-block mechanisms, where changes of the crystalline lens with age, as increasing thickness and forward movement, result in increased iridolenticular contact with increased trans-pupillary aqueous flow resistance, may contribute to this phenomenon.

In ▶ acute angle closure, circumferential apposition of the iris to the trabecular meshwork causes rapid and excessive increase in IOP.

In contrast, in intermittent angle closure, clinical symptoms are milder as the iridotrabecular apposition is transient and resolves spontaneously.

Chronic angle closure may develop after an acute attack in which synechial closure persists or may also develop when the chamber angle closes gradually with slow formation of PAS, which advance circumferentially. In such creeping ▶ angle closure, multiple mechanisms are suspected to be involved, including pupillary block and ▶ plateau iris.

Clinical Presentation

▶ Acute primary angle closure presents with unilateral ocular pain and headache, red eye, mild dilated and non-reactive pupil, iris bombé, photophobia, decreased or blurred vision and halos, disc edema, and splinter hemorrhages, but also with nausea and vomiting, and occasionally abdominal cramps and palpitations.

Typically, patients who develop primary angle closure have symmetric small, "crowded" anterior segments, a shallow anterior chamber, and short axial lengths. Hyperopia may also be present. Asymmetry of anterior chamber depth is highly suspicious of secondary angle closure.

Intermittent or subacute angle closure is characterized by recurrent episodes of blurred vision, halos, and mild pain due to elevated IOP. In contrast to acute angle closure, these symptoms resolve spontaneously – often during sleep – and can therefore be misinterpreted as headache or migraine. Between episodes, the IOP may be normal. Otherwise, there may be signs of previous

attacks including a permanently fixed, mid-dilated pupil, sector iris atrophy, pigmentary dusting of the corneal endothelium, anterior subcapsular lens opacities (so-called glaukomflecken), PAS, and manifest GON.

Intermittent angle closure may also progress to chronic angle closure.

Chronic angle closure is typically asymptomatic. In the course of disease, mild to moderate elevation of IOP results in GON and corresponding visual field defects.

Diagnosis

▶ Angle closure is diagnosed on gonioscopy, preferably by dynamic gonioscopy to distinguish between appositional angle closure and peripheral synechiae.

In primary angle closure, gonioscopy reveals a narrow anterior chamber angle in both the affected and fellow eye; a significant difference in anterior chamber depth is suggestive of ▶ secondary angle closure glaucoma.

In chronic angle closure, dynamic gonioscopy may reveal PAS in patients with modest elevation of IOP and GON.

▶ Ultrasound of the anterior segment may reveal additional structural changes of the peripheral iris or ciliary body.

Tonometry reveals elevated IOP.

Biomicroscopy with accurate assessment of the anterior chamber as well as the posterior segment is mandatory in classifying the various forms of angle closure and angle closure glaucoma. Previous ocular and medical history, family history as well as subjective symptoms should be inquired to exclude or confirm previous attacks in case of acute or intermittent angle closure.

▶ Visual field examination, retinal nerve fiber layer assessment, and optic disc imaging should be performed to assess the stage of disease.

Differential Diagnosis

For differential diagnosis, consider any secondary angle closure with elevated IOP, either neovascular glaucoma, ▶ uveitic glaucoma, ▶ lens-induced angle closure, and angle closure due to aqueous misdirection (▶ malignant glaucoma) or to choroidal pathologies (e.g., ▶ uveal effusion).

Also consider any ▶ secondary open-angle glaucoma with acute rise of IOP like inflammatory, ▶ corticosteroid glaucoma, ▶ Posner-Schlossman syndrome, ▶ pseudoexfoliative glaucoma, ▶ pigmentary glaucoma, ▶ ghost cell glaucoma, ▶ phacolytic glaucoma, or open-angle glaucoma due to intraocular malignant tumors.

Prophylaxis

There is clear evidence for prophylactic treatment in fellow eyes of acute angle closure.

Therapy

Therapy of primary angle closure and angle closure glaucoma depends on the clinical presentation and stage of disease.

In acute primary angle closure, medical treatment includes mild topical ▶ miotic agents; topical hypotensive medication like ▶ beta-blocker, alpha agonists, and ▶ prostaglandin analogues; topical steroids to prevent PAS formation; and systemic aqueous humor suppressants, either ▶ carbonic anhydrase inhibitors or hyperosmotic agents. Indentation of the cornea may open the anterior chamber angle by shifting the fluid in the anterior chamber into the periphery.

The definitive treatment for acute primary angle closure is iridectomy either laser or surgical. In some cases, peripheral laser iridoplasty may be necessary prior to iridectomy to flatten the peripheral iris.

Another approach is surgical lens extraction, especially in cases where a lens-block mechanism is involved.

In intermittent and chronic angle closure, a laser iridotomy may relieve a pupillary block component and reduce the risk of further permanent synechiae. Nevertheless, the disease may progress, and long-term use of topical hypotensive medication or even filtering surgery may be indicated to lower IOP.

Prognosis

Angle closure glaucoma accounts for 50% of all glaucoma blindness worldwide and is probably the most visually destructive form of glaucoma.

Besides the above-described mechanism of direct obstruction, often with rapidly developing peripheral anterior synechiae, primary angle closure may impair aqueous outflow also by causing irreversible degeneration and damage of the trabecular meshwork during phases of raised IOP.

After an acute attack, IOP may be lowered due to reduced aqueous humor production after ischemia of the ciliary body. Therefore, repeated gonioscopy is mandatory to confirm a persistent open angle.

There is a 40–80% risk of acute angle closure in the fellow eye.

Prognosis for intermittent and chronic primary angle closure depends on the extent of optic nerve damage and subsequent IOP control.

Epidemiology

Primary angle closure is rare in individuals younger than 40, and the prevalence increases with each decade after 40 years of age. It is 2–4 times more common in women than men. The prevalence of primary angle closure in patients older than age 40 varies depending on ethnicity and is highest in Inuit with 2.1–5.0%, followed by East Asians (0.3–1.4%) and Japanese (0.3%), whereas it is only 0.1–0.6% and 0.1–0.2% in Caucasian and black populations, respectively. The prevalence is also increased in first-degree relatives of patients with primary angle closure, with the highest relative risk in Chinese, followed by Inuit.

Caucasians present more commonly with acute forms, whereas Africans and Asians present more frequently with asymptomatic chronic disease. Chronic open-angle glaucoma is the major cause of irreversible blindness in Asia.

Cross-References

- ▶ Acute Angle Closure
- ▶ Altitudinal Visual Field Defects
- ▶ Angle Closure
- ▶ Angle Closure Secondary to Uveal Effusion
- ▶ Angle-Closure Glaucoma
- ▶ Beta Carotene, Use and Dosage of
- ▶ Carbonic Anhydrase Inhibitors, for Cystoid Macular Edema
- ▶ Ghost Cell Glaucoma
- ▶ Iridotomy
- ▶ Lens-Induced Angle-Closure Glaucoma
- ▶ Malignant Glaucoma
- ▶ Pigmentary Glaucoma
- ▶ Posner-Schlossman Syndrome
- ▶ Prostaglandin Analogues
- ▶ Pseudoexfoliative Glaucoma
- ▶ Secondary Open-Angle Glaucoma
- ▶ Uveitic Glaucoma

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Primary Angle Closure Suspect

- ▶ Angle-Closure Suspect

Primary Color Vision Deficiency

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Synonyms

Inherited color vision disorders; Inherited dyschromatopsia

Definition

Normal color vision in human observers is trichromatic, depending upon three populations of cone photoreceptors, each containing a visual pigment with a different absorption spectrum. Primary inherited color vision deficiency arises from mutation in one or more of the genes coding the three types of cone visual pigments. There are several characteristics typical to primary inherited color vision deficiency which separate it from acquired color deficiency: (i) the color vision defect is present from birth and does not change with age, (ii) it is symmetrical in the two eyes, (iii) it is well defined by the commonly used color vision tests, and (iv) in most cases, there is no additional retinal involvement.

Structure

Primary inherited color vision deficiency arises from a mutation in one or more of the genes coding the protein part of the cone visual pigments. There are three genes involved; two of them, the genes coding the long-wavelength and the medium-wavelength visual pigments, are located on the X chromosome (L-gene and M-gene, respectively) and are arranged in a head-to-tail tandem. The short-wavelength visual pigment is coded by the S-gene, located on chromosome 7.

On the X chromosome, a single L-gene is followed by one or more M-genes. The number of M-genes is polymorphic; approximately 25% of male Caucasians have a single M-gene, 50% have two M-genes, and the remainders have three or more M-genes. Regardless of the number of M-genes, only the first two genes coding visual pigments are expressed (L-gene and M-gene).

The L-cone opsin gene and M-cone opsin gene contain six exons, which are highly homologous and share 96% amino acid identity, while their homology to the S-cone opsin gene and to the rod opsin gene is approximately 40%. Due to their proximity and high similarity of their sequences, the genes coding for the L-cone opsin and the M-cone opsin are highly subject to unequal recombination resulting in chimera (hybrid) genes. When one of the first two cone opsin genes on the X chromosome is a chimeric gene, color deficiency in the red-green part of the spectrum is present. A color vision disorder in the blue region of the spectrum requires mutation in the S-cone opsin gene located on chromosome 7. Mutations in the S-cone genes are transmitted by autosomal dominant inheritance mode, characterized by either complete penetrance, or almost complete penetrance or incomplete penetrance depending upon the exact mutation.

The majority of patients with inherited color vision defects suffer from absence or abnormality in one or both of the cone opsin genes on the X chromosome, leading to inactive or abnormal light absorption by the corresponding cones. Therefore, color vision disorders in the red-green part of the visible spectrum are more prevalent in males than in females. A total of about 8% in males and 0.01% in females suffer from red-green color vision deficiency. Color vision deficiencies in the blue part of the spectrum is equally divided between males and females and are rare, appearing in about 1 out of 10,000 of the population.

Function

Trichromatic color vision means that a mixture of three primary colors can reproduce any color. When color vision is tested in the laboratory, the subject is seated in front of a colorimeter and observes a bipartite visual field. One half contains a monochromatic light of any wavelength within the visible range (400–700 nm) having a fixed intensity, while the other half contains a mixture of three primaries (e.g., 450 nm, 540 nm, and 600 nm for blue, green, and red primaries, respectively). The observer is instructed to adjust the intensities of the three primaries (one of them can be moved, if needed, to the other half of the field), until the two halves of the field appear indistinguishable from one another. This is called metameric color matching. An observer with normal color vision (trichromatic) needs to adjust the intensity of all three primaries in order to reach a

metameric color match, and the relationships between the intensities of the three primaries is remarkably similar between observers with normal trichromatic color vision. Metameric color matching means that the total numbers of photons absorbed by the L-cones, by the M-cone, and by the S-cones are identical in both sides of the visual target. Therefore, metameric color matching depends only upon the spectral properties for light absorption by the cone visual pigments, and not upon the relative number of L-cones to M-cones to S-cones. Patients suspected of suffering from primary inherited color vision deficiency are tested on the colorimeter in order to define their type of color vision defect. There are three major types of inherited color vision defects:

i. *Anomalous trichromacy*: The anomalous trichromats need to adjust the intensities of the three primaries in order to obtain a metameric match to any test wavelength, but their match differs from that of the normal trichromat. If the long-wavelength pigment differs from the normal one (protanomaly), the patient will need a different intensity for the red primary for a match compared to the normal observer. The deuteranomalous, whose medium-wavelength cone visual pigment differs slightly from that of the normal one, will need a different intensity of the green primary for a match, and the tritanomalous will need a different intensity for the blue primary to achieve a metameric color match compared to the normal trichromat. In general, the anomalous trichromat will not accept the color match of a normal trichromat, and a normal trichromat will not accept the color match of the anomalous trichromat.

   These patients have three functional cone opsin genes, but one of them differs and codes an abnormal cone opsin. Chimeric visual pigments genes in the X chromosome are associated with two types of anomalous trichromacy, deuteranomaly, and protanomaly. Thus, if the first gene is a normal L-cone gene, and the second is an L-chimeric gene, coding for a visual pigment that differ slightly in peak absorption from the normal L-cone gene, the individual will be a deuteranomalous. In contrast, when the L-cone gene is missing and the first two genes code a normal M-cone gene and a chimeric one that codes for an M-cone gene, having different peak absorptions than the normal M-cone gene, the individual will be a protanomalous. The degree of anomalous trichromacy in the red-green part of the visible spectrum ranges from very severe to mild depending upon the distance between the peak absorptions of the two existing cone visual pigments, the larger the difference the milder is the defect. In tritanomaly, the visual pigments in L-cones and M-cones are normal, while the absorption spectrum of the S-cone visual pigment differs slightly from that of the normal color vision observer. Protanomaly appears in 1.08% and deuteranomaly in 4.63% of the male population. Tritanomaly is a rare defect appearing in 1 of 10,000 of the general population.

ii. *Dichromacy*: These individuals miss one of the cone visual pigments, but the existing two pigments are normal. Protanopes miss the long-wavelength cone visual pigment, deuteranopes miss the medium-wavelength cone visual pigment, and tritanopes miss the short-wavelength cone visual pigment. These individuals are called dichromats because they need to adjust the intensity of two primaries in order to make a metameric color match to any monochromatic light of fixed intensity. Since they have normal two cone visual pigments, they will accept the color match of a normal trichromat, but the trichromat will not accept the metameric color match of the dichromat because one of the primaries has not been adjusted. Protanopia is present in 1.01% and deuteranopia in 1.27% of the male population, while tritanopia is more rare, appearing in 1 out of 10,000 of the normal population. In fact, because the center of the fovea, to foveola, lacks short-wavelength cones, every individual with normal trichromatic color vision behaves as a tritanope when colored objects illuminate only the foveola.

iii. *Monochromacy*: These are divided into cone monochromats and rod monochromats. Cone

monochromats possess two types of functioning photoreceptors, one spectral type of cones and rods. Rod monochromats contain only one type of functioning photoreceptors, the rod photoreceptors. Cone monochromats can slightly distinguish between colors under mesopic conditions (dusk) when both cones and rods function in parallel and therefore are said to suffer from incomplete achromatopsia. Rod monochromats suffer from complete color blindness and see only shades of gray. Therefore, they are said to suffer from achromatopsia. The big difference between the two types is expressed in daytime vision. Cone monochromats can function under wide range of background luminance, and they are not photophobic. Red-cone monochromats and green-cone monochromats enjoy relatively good visual acuity, while blue-cone monochromats have poor visual acuity because the foveola, the center of the fovea, lack blue cones, and thus there are no functioning cones in the center of the fovea of blue-cone monochromats. Rod monochromats suffer from photophobia, they are "afraid of light" under background conditions, and they have poor visual acuity. Monochromats are very rare; the most prevalent type is the blue-cone monochromat, appearing in about 1 in 100,000 affecting mainly males, since they suffer from mutations in the red-opsin and green-opsin genes located next to each other on the X chromosome. Red-cone monochromats and green-cone monochromats require mutation in one of the cone opsin genes on the X chromosome, and mutation of the blue-opsin gene in both alleles of chromosome 7. This is a very rare situation and some estimate as 1 in 1,000,000 while others believe it is even more rare, 1 in 100,000,000. Rod monochromats, caused by mutations in all three cone opsin genes are very rare, more rare than the red-cone monochromats and the green-cone monochromats. The most common cause of rod monochromatism (achromatopsia) is a mutation in a specific gene that code proteins specific for the phototransduction process of cones and not of rods. Mutations in GNAT2 (the cone transducin), PDE6C (the cone phosphodiesterase), or CNGB3 (the cone cGMP-dependent cationic channels) were found to be associated with achromatopsia, with the latter being the most prevalent one. Individuals, suffering from one of the above mutations, have all three spectral types of cones containing normal visual pigments, but light absorption is not translated to electrical activity, and therefore, there is no visual perception from the cone system. The prevalence of rod monochromatism (achromatopsia) is 1 in 33,000–50,000.

Clinical Relevance

Color vision deficiency may impose a disadvantage when performing visual tasks, requiring distinction between the colors of an object embedded in its background, such as the detection of fruit among foliage. Subjects with red-green color defects complain on difficulties navigating in the color-coded world of Internet; they have difficulties distinguishing traffic lights and also choosing clothing of matching colors. For certain professions where safety of people or quality of products may be affected, specific vocational tests are used to assess for normal color vision. Thus, children with inherited color vision defects need to be discouraged from planning on becoming police officers, sailors, pilots, and more. Young children with inherited color defects may encounter difficulties during their education since colors play an important role as cues during reading or math teaching. The most serious problems arise when color vision disorders are misinterpreted as learning difficulties.

In medical practice, though there is no evidence of adverse outcome, there are reports of physicians misdiagnosing clinical signs such as rashes and jaundice and ophthalmologists confusing blood and pigment on ophthalmoscopy.

Despite these disadvantages, primary color deficiency is maintained at high rate in the population, suggesting it may also confer an advantage. Some evidence suggests that patients suffering from anomalous trichromacy can break

camouflages, which confounds subjects with normal trichromatic color vision.

Cross-References

- ▶ Absorption, Light, Spectra of Visual Pigments
- ▶ Anomalous Trichromats
- ▶ Blue Cone Monochromatism
- ▶ Color Vision, Three Cone Opsins
- ▶ Day Blindness (Hemeralopia), in Cone Dystrophies
- ▶ Photoreceptor Cells

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Primary Congenital Glaucoma

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Definition

Primary congenital glaucoma (PCG) is the most common type of developmental glaucoma in infants and children and results from an isolated abnormality in the filtration angle during gestation in the absence of other ocular anomalies.

Synonyms

Developmental glaucoma; Infantile glaucoma; Isolated trabeculodysgenesis

Etiology

Although it is generally accepted that abnormal development of the anterior chamber angle results in obstruction of aqueous outflow facility and elevated intraocular pressure (IOP), the exact pathogenesis of PCG remains unclear. Initial suggestion of a Barkan's membrane lining the anterior chamber angle recess has not been histopathologically proven. There appears to be a developmental arrest of anterior chamber angle tissues derived from neural crest cells. The high insertion of the ciliary body and iris may compress the underlying trabecular meshwork beams (Anderson 1981). The trabecular beams have also been described to be thickened, affecting aqueous outflow facility. In addition, immaturity of the juxtacanalicular meshwork and underdevelopment of Schlemm's canal have been described.

Epidemiology and Genetics

The incidence varies widely from 1 in 10,000 live births in the United States to about 1 in 1250 live births in Romanian gypsies, with overall incidence increasing with consanguinity. Most cases are sporadic with 10–40% reported to be familial. In familial cases, autosomal recessive inheritance with variable expression is the most common mode of transmission. Several chromosomal loci for PCG have been identified: GLC3A (chromosome 2), GLC3B (chromosome 1), GLC3C (chromosome 14), and GLC3D (14q24). However, only two genes have been identified: cytochrome P4501 subfamily 1B1 (CYP1B1) on the GLC3A locus and latent transforming growth factor beta-binding protein 2 (LTBP2) on the GLC3D locus (Mauri et al. 2016). The CYP1B1 protein is a membrane-bound monomeric monooxygenase that is thought to be involved in the metabolism of a yet-unidentified compound that regulates development of the anterior chamber angle, particularly the trabecular meshwork. Several mutations in CYP1B1 gene have been identified, including point missense, nonsense, frameshift, terminator mutations, deletion, and

insertion with significant heterogeneity (Abdolrahimzadeh et al. 2015). Mutations in one gene, CYP1B1, on locus GLC3A were reported in 87% of familial cases of PCG in contrast to 27% in sporadic cases (Sarfrazi and Stoilov 2000). LTBP2 mutation is rare and has been reported in few families in Pakistan, Iran, and European Gypsies. Autosomal dominant inheritance caused by hypo- and hypermorphic FOXC1 has also been reported (Medina-Trillo et al. 2016).

Clinical Presentation

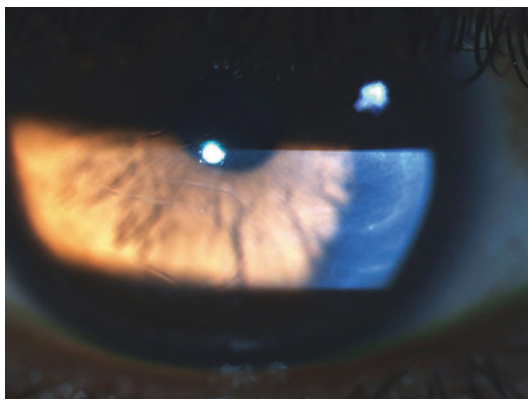
These cases are typically bilateral with male predominance and are usually diagnosed at birth or within the first year of life. The classic symptoms include epiphora, photophobia, and blepharospasm. These symptoms result from horizontal breaks (Fig. 1) in Descemet's membrane (Haab striae) and associated corneal edema, which in turn result from elevated IOP. The distensibility of the neonatal globe results in enlargement of the cornea, sclera, optic nerve, and lamina cribrosa (Allingham et al. 2005). Once buphthalmos develops (Fig. 2), the globe does not return to its normal size with normalization of IOP. The increased axial length results in myopia, which can lead to amblyopia in unilateral and asymmetric cases.

Clinical Examination

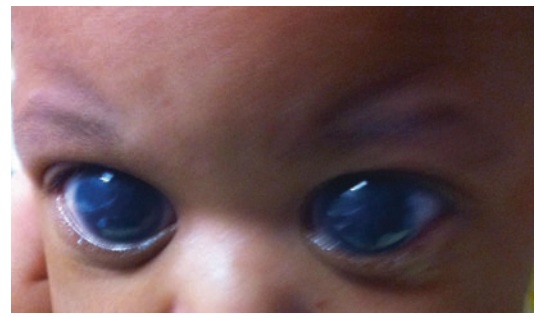
Key examination components include vision assessment, tonometry, measurement of central corneal thickness (CCT) and corneal diameter, anterior segment examination (with emphasis on cornea, anterior chamber depth, iris, and pupil), gonioscopy, ophthalmoscopy, ultrasonography, and retinoscopy. The IOP should be measured soon after induction of anesthesia to avoid influence on measurements by various anesthetic agents. Corneal diameter and CCT are usually inversely related. Gonioscopy is critical for both diagnostic and therapeutic decisions. Typical findings include a high iris insertion with limited view of the angle recess, peripheral iris hypoplasia, and thickened and stippled appearance of the trabecular meshwork. In infants and children, the cup enlarges circumferentially with enlargement of the scleral canal, and optic nerve cupping may be reversible.

Differential Diagnosis

Differential diagnoses include nasolacrimal duct obstruction, conjunctivitis, megalocornea, axial myopia, obstetric trauma, corneal opacification from infections and dystrophies, inborn error of metabolism (mucopolysaccharidosis), physiologic optic nerve cupping, optic nerve coloboma, and optic nerve atrophy.



Primary Congenital Glaucoma, Fig. 1 Haab striae – horizontal breaks in Descemet's membrane



Primary Congenital Glaucoma, Fig. 2 Buphthalmos, enlarged globes with megalocornea

Management and Prognosis

PCG is a surgical condition with medical therapy serving as a temporizing measure before surgery or playing an adjunctive role after surgery (Allingham et al. 2005). Beta blockers and carbonic anhydrase inhibitors are generally effective. Alpha agonists should not be used in infants and young children, given reports of bradycardia, apnea, hypothermia, hypotension, and hypotonia. Cholinergic agents may paradoxically increase IOP because of high insertion of the ciliary muscle into the trabecular meshwork. Literature is limited on the use of prostaglandin analogues in infants with better efficacy reported in older children. Angle surgery, either goniotomy or trabeculotomy, creates a direct communication between the anterior chamber, and SC and is reported to be successful in 70–80% of cases in the United States (Salim and Walton 2008), but with lower success rates in developing countries. Other surgical alternatives include trabeculectomy with or without antimetabolites, combined trabeculotomy and trabeculectomy, glaucoma drainage implants, and cyclophotocoagulation for intractable cases with poor visual potential. Associated amblyopia should be aggressively treated. Life-long follow-up is needed, because IOP elevation may recur at any age.

Cross-References

- ▶ Childhood Glaucoma
- ▶ Corneal Diameter
- ▶ Descemet's Membrane Endothelial Keratoplasty (DMEK)
- ▶ Infantile Glaucoma
- ▶ Myopic Chorioretinal Atrophy and Lacquer Cracks

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Primary Endothelial Failure, After Penetrating Keratoplasty

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P

Synonyms

Primary graft failure

Definition

Corneal graft edema starting on the first postoperative day which does not clear within 2 months (Mannis et al. 2013).

Etiology

The most common etiology is usually a low endothelial cell count, often from manipulation of the graft during surgery (Wilhelmus et al. 1995). Other causes include postoperative inflammation, hypotony, glaucoma, and vitreous and iris adhesions to the endothelium. For endothelial

keratoplasties, poor adhesion at the graft-host interface is another cause.

Occurrence

Occurs in approximately 1% of graft failures (Mannis et al. 2013).

Classification

For penetrating keratoplasties, primary failure consists of grafts that do not clear postoperatively. For endothelial keratoplasties, they are grafts that do not reattach or never clear postoperatively (Oster et al. 2009). Both present with microcystic edema, often with Descemet's folds. Patients often complain of blurry vision and may have foreign body sensation and photophobia.

Cross-References

▶ Endothelial Graft Rejection
▶ Transplantation

References

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Primary Graft Failure

▶ Primary Endothelial Failure, After Penetrating Keratoplasty

Primary Hereditary Systemic Amyloidosis

▶ Meretoja Syndrome

Primary Intraocular Lymphoma

▶ Intraocular Lymphoma

Primary Open-Angle Glaucoma

▶ High-Pressure Glaucoma

Primary Pigmentary Retinal Degeneration

▶ Retinitis Pigmentosa, Decreased Vision in Neuro-Ophthalmology

Primary Posterior Capsulorhexis

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Synonyms

Primary posterior continuous curvilinear capsulorhexis

Definition

An operative technique in cataract surgery to prevent posterior capsule opacification (PCO). It is based on the theory that by removing the scaffold

for the migration of lens epithelial cells, a permanently clear optical zone can be provided. Primary posterior capsulorhexis can be performed in combination with anterior vitrectomy and is a common procedure in the treatment of congenital cataract. A planned primary posterior capsulorhexis is also useful in removing posterior capsular plaques and can also be attempted when a small posterior capsular rupture occurs to prevent radial extension of the tear.

History

In 1990 Gimbel et al. suggested that a posterior capsulorhexis is useful in three different situations: for the prevention of a posterior capsule tear, in the presence of a posterior capsule plaque, and in infants because the risk of development of a posterior capsule opacification is high. In such cases it is difficult to perform laser. In 1993 Galand et al. began performing a technique of primary posterior capsulorhexis in adult eyes with intact and clear posterior capsules. Recently Menapace used this method combined with optic buttonholing in a large series of patients to prevent posterior capsule opacification with budding results.

Clinical Features

Posterior capsule opacification is a common problem in cataract surgery. The effect of this opacification is a severe decrease in vision acuity. The treatment of posterior opacification is a postoperative neodymium: YAG (Nd:YAG) capsulotomy of which the rate of retinal detachment has been reported from 0.50% to 4.16%. This side effect led to the idea of preventing a posterior capsular opacification by removing a part of the posterior capsule intraoperatively.

Tests

In order to achieve best postoperative results, thorough slit-lamp examination with dilated pupil, Scheimpflug imaging and measurement of uncorrected and best spectacle-corrected visual acuity are essential.

Etiology

See "History" section above.

Differential Diagnosis

Another nonsurgical type of treatment of posterior capsular opacification is:

– Neodymium: YAG (Nd:YAG) capsulotomy

Treatment

At the end of cataract or refractive lens removal, the posterior capsulorhexis can be performed. A layer of sodium hyaluronate (Healon) should be placed on the posterior capsule after which a central opening of the posterior capsule can be performed. Through this opening a generous layer of sodium hyaluronate is injected to separate the posterior capsule of the anterior vitreous. Then a central piece of the capsule can be excised to obtain a posterior capsulorhexis of 3–4 mm in diameter. Sodium hyaluronate can then be used to separate the anterior and posterior capsule and the intraocular lens can be implanted.

Cross-References

▶ Anterior Vitrectomy
▶ Posterior Capsule Opacification (PCO)
▶ Posterior Optic Buttonholing

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Primary Posterior Continuous Curvilinear Capsulorhexis

▶ Primary Posterior Capsulorhexis

PRK

▶ Photorefractive Keratectomy (PRK)
▶ Phototherapeutic Keratectomy

PRL

▶ PRL Phakic Intraocular Lens

PRL Phakic Intraocular Lens

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Synonyms

Phakic refractive lens; Posterior chamber phakic intraocular lens; PRL

Definition

A phakic IOL that is placed between the iris and the crystalline lens floating freely over the crystalline lens.

Epidemiology

Today, the number of implanted PRLs is not high in relation to the latest anterior chamber phakic IOL model (AcrySof) and the iris-supported phakic IOL models (Artisan/Verisyse and Artiflex/Veriflex) (Güell et al. 2010).

History

Complications from anterior chamber angle-supported implants led to the idea of moving toward the posterior chamber. This location theoretically provided lower incidence of halos and glare as the margins of the pupil cover the border of the optical zones. Additionally, the risk of corneal endothelial damage was also theoretically minimized, due to the greater distance between the implant and the corneal endothelium. One of the first posterior chamber phakic IOL designs, the "collar-button" or "mushroom" configuration, is attributed to Fyodorov in 1986 (Hardten et al. 2003). He developed a one-piece silicone lens, with a 3.2-mm optic and a concave anterior surface that projected anteriorly through the pupil. The lens was fixated behind the iris plane by two haptics and had a total length of 8.0 mm. Initial complications included corneal touch, decentration, pupillary block glaucoma, iridocyclitis, and cataract formation (Kohnen and Koch 2006). Since then, evolution in design and materials has led to the emergence of several different models, including the Adatomed lens. However, cortical opacities and decentration frequently occurred after surgery, and this lens was also withdrawn from the market. Currently, there are only two posterior chamber models available on the market: the "implantable contact lens" (ICL, STAAR Surgical, Monrovia, USA) and the "phakic refractive lens" (PRL, Carl Zeiss Meditec, Jena, Germany).

Clinical Features

The foldable PRL can be used for the correction of myopia and hyperopia and is made of hydrophobic silicone. It has a concave posterior base curve of 10-mm radius that mimics the anterior curvature of the crystalline lens. Central thickness is less than 0.5 mm and is constant for myopic lenses but varies with hyperopic lenses. Edge thickness is always less than 0.2 mm, and it is constant in hyperopic and varies in myopic lenses. There are two models of myopic lenses available: overall diameter of 10.8 mm (PRL 100) and 11.3 mm (PRL 101). Diameter of the optic is 4.5–5.5 mm, depending on the lens power, which ranges from −3.0 to −20.0 D - (maximum correction at the spectacle plane of −28 D). Hyperopic lenses (PRL 200) have an overall diameter of 10.6 mm, a 4.5-mm optic, and power ranges from +3.0 to +15.0 D. Because this type of PIOL lacks fixation, stability of centration and rotation is of concern. Thus, this lens is unsuitable for the correction of astigmatism.

Tests

Anterior chamber depth for PRL implantation must be at least 2.5 mm. Other inclusion criteria for phakic IOL implantation must be considered (see also "► Phakic Intraocular Lens").

Differential Diagnosis

The other posterior chamber phakic IOL is the ICL that is fixated in the ciliary sulcus.

Etiology

Other currently available types of phakic IOLs are anterior chamber angle- (AcrySof) or iris-supported phakic IOLs (Artisan/Verisyse and Artiflex/Veriflex).

Treatment

Implantation procedure for the PRL is almost the same as for the ICL. Two opposed paracentesis ports are created on either side of a 3.2-mm clear cornea incision. The PRL is inserted with a specially designed forceps or with an injector system. As the lens unfolds slowly in the anterior chamber, its haptics initially lie anterior to the dilated iris. Each haptic corner then is gently placed behind the iris through the pupil with a long spatula or an intraocular hook. When proper horizontal lens orientation is verified, a miotic agent is injected. As spontaneous rotation of the PRL may easily occur, two peripheral iridotomies, 90° apart, are mandatory to prevent pupillary block situation.

Cross-References

- ► Foldable Intraocular Lens
- ► Intraocular Lens
- ► Phakic Intraocular Lens
- ► Silicone Intraocular Lens
- ► Verisyse Iris-Supported Phakic Intraocular Lens

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Progressive Iris Atrophy

► Iridocorneo Endothelial Syndrome

Progressive Pigmentary Retinopathy

▶ Retinitis Pigmentosa, Decreased Vision in Neuro-Ophthalmology

Progressive Supranuclear Palsy

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Synonyms

Steele-Richardson-Olszewski Syndrome

Definition

Progressive supranuclear palsy (PSP) is a neurodegenerative disease characterized by a progressive, bilateral supranuclear ophthalmoplegia and postural instability. The clinical and neuropathological features of this disease were first described in a nine patient study by Steele, Richardson, and Olszewski in 1964. It is considered to be the most common of the atypical Parkinsonian syndromes, which include multiple systems atrophy (MSA) and corticobasal degeneration (CBD).

Etiology

The underlying cause of PSP is unknown, but a combination of genetic, environmental, and inflammatory factors likely contributes. The pathogenesis involves neuronal loss, gliosis, and accumulation of neurofibrillary tangles in various regions of the brain, most commonly the basal ganglia, diencephalon, brainstem, and cerebral cortex. PSP is considered to be a tauopathy, a group of neurodegenerative diseases that includes CBD, Pick disease, frontotemporal dementia, and Alzheimer disease. Tauopathies are defined by the pathological aggregation of tau proteins, which normally function in the central nervous system to stabilize microtubules and facilitate axonal transport. Abnormal phosphorylation of these tau proteins leads to misfolding and subsequent self-aggregation into neurofibrillary tangles. The exact role of neurofibrillary tangles in tauopathies like PSP is still unclear, but in general, they seem to be correlated with disease progression. In PSP, the neurofibrillary tangles are uniquely composed of straight filaments of tau protein, which distinguishes it from other tauopathies.

While PSP is considered to be a sporadic disease, some studies have identified familial aggregations of PSP with autosomal dominant inheritance pattern. Other studies have indicated that certain mutations in the microtubule-associated protein tau gene (MAPT) may be a significant risk factor for the sporadic form of the disease.

Clinical Presentation

Classic PSP is the most common and well-known form of PSP. The most common initial manifestation of classic PSP is gait disturbance, which leads to frequent falls and traumatic injuries. Approximately 69% of patients report mobility issues at

disease onset. Many patients will also develop some kind of personality or cognitive change within 2 years of disease onset. The progressive, supranuclear ophthalmoplegia (the hallmark of PSP) generally develops within 3–4 years of disease onset but can take as long as 10 years. The slowing of vertical saccades is often the first visual manifestation seen in PSP and helps contribute to initial diagnosis. Other prominent features of classic PSP include axial rigidity, dysarthria, dysphagia, and sleep disturbances. In contrast to the more common and often age-related, supranuclear upgaze palsy, a supranuclear downgaze palsy in an older patient is always pathologic and should raise the suspicion for PSP.

Several different clinical subtypes of PSP have been described, including PSP-Parkinsonism (PSP-P), PSP-pure akinesia with gait freezing (PSP-PAGF), and PSP-primary progressive freezing gait (PSP-PPFG). These atypical subtypes of PSP typically do not satisfy all of the diagnostic criteria for classic PSP and have their own unique features. The atypical subtypes of PSP also tend to have a better prognosis than classic PSP.

Diagnostics

The National Institute of Neurological Disorders and Stroke (NINDS) and the society for PSP (SPSP) proposed a set of diagnostic criteria for PSP in 1996, which includes different criteria for "possible, probable, and definite" PSP as well as mandatory exclusion criteria. Important inclusion criteria for PSP include gradually progressive disorder, age of onset greater than 40 years, and vertical supranuclear palsy and/or prominent postural instability within the first year of disease onset. Definitive diagnosis however requires neuropathological examination (although it is generally not performed). Exclusion criteria are designed to rule out iatrogenic, inflammatory, infectious, and structural disease as well as other neurodegenerative diseases that can mimic PSP.

Unfortunately, there are no established laboratory or imaging findings for the diagnosis of PSP. Magnetic resonance imaging (MRI) or computed tomography (CT) of the brain may however demonstrate atrophy of the affected areas, especially the midbrain ("the hummingbird sign"), and may support diagnosis of PSP.

Differential Diagnosis

PSP is most commonly confused with other Parkinsonian disorders. The differential diagnosis of PSP includes idiopathic Parkinson disease, corticobasal degeneration, multiple system atrophy, dementia with Lewy bodies, vascular Parkinsonism, Alzheimer disease, Creutzfeldt-Jakob disease, and central nervous system (CNS) whipple disease.

Therapy

There is currently no effective therapy for PSP.

Prognosis

The prognosis for PSP is quite poor, as median survival from time of diagnosis ranges from 6 to 12 years. Shorter time to certain clinical milestones, including frequent falls, cognitive disability, unintelligible speech, and wheelchair dependence, is associated with poorer prognosis. Patients also experience significant decline in quality of life as the disease progresses, with symptoms like immobility and cognitive impairment being especially debilitating. The atypical PSP syndromes tend to progress slower and have a better prognosis than classic PSP.

Epidemiology

The prevalence of PSP is disputed due to the diagnostic challenges it presents, but studies from the UK in 1999 show rates as high as 6.4 per 100,000. An earlier study from the USA in 1988 demonstrated prevalence of 1.39 per

100,000, but it is believed that the real number is actually higher with the recent discovery of the PSP subtypes. The mean age of onset for PSP is about 62 years old.

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Proliferative Endotheliopathy

► Iridocorneo Endothelial Syndrome

Proliferative Retinopathy due to Diabetes

► Diabetic Retinopathy, Proliferative

Proptosis

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Synonyms

Exophthalmos (when associated with thyroid eye disease)

Definition

Proptosis is defined as the forward protrusion of one or both globes.

Etiology

The most common cause of proptosis is thyroid eye disease. Other causes of proptosis include infection (orbital cellulitis, mucormycosis, concurrent sinus disease), inflammatory disease (orbital inflammatory pseudotumor, posterior scleritis), vasculitis (Wegener's granulomatosis, polyarteritis nodosa), neoplasm (lacrimal, lymphoma, leukemia, meningioma, glioma, rhabdomyosarcoma, metastatic), orbital vascular disease (orbital varix, carotid-cavernous sinus fistula, arteriovenous malformation), and trauma (retrobulbar hemorrhage, orbital or facial fractures).

Occurrence

Proptosis can be diagnosed with exophthalmometry, which measures the distance between the lateral angle of the bony orbit and the cornea. A difference of at least 2 mm between the two eyes of any given patient is considered abnormal. Normal upper limits for proptosis are approximately 22 mm in Caucasians and 24 mm in African-Americans. The amount of proptosis

can also be quantified by measuring globe protrusion on CT scan.

Proptosis occurs in both adults and children at any age. Thyroid orbitopathy and the resultant exophthalmos in 60% of patients show a female preponderance with a female to male ratio of 6:1 and a predilection for middle-aged adults (30–50 years).

Classification

Proptosis can be classified by unilateral or bilateral involvement. The most common cause of unilateral and bilateral proptosis in adults is thyroid eye disease. Most tumors present as unilateral proptosis. However, bilateral orbital involvement from lymphoma, vasculitis, idiopathic orbital inflammatory disease, metastatic tumor, or leukemia can also produce bilateral proptosis. In children, unilateral proptosis is often due to infectious causes, and in bilateral cases, metastatic neuroblastoma, leukemia, or idiopathic orbital inflammatory disease is more likely.

Proptosis can also be classified by axial or nonaxial displacement of the globe. Axial displacement is caused by retrobulbar lesions such as cavernous hemangioma, glioma, meningioma, metastases, and any other mass lesions within the muscle cone. Nonaxial or eccentric displacement is caused by extraconal lesions in which the direction of proptosis is determined by the site of the mass including maxillary sinus tumors, lacrimal gland tumors, and frontoethmoidal mucoceles.

Cross-References

- ▶ Globe, Displacement of, in Orbital Disorders
- ▶ Graves' Disease
- ▶ Orbit, Inflammation of
- ▶ Pseudoproptosis

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Prostaglandin Analogues

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Synonyms

Prostanoids

Definition

A class of medications used to lower intraocular pressure by increasing uveoscleral outflow through activation of prostaglandin receptors and includes the medications latanoprost, bimatoprost, and travoprost.

Cross-References

- ▶ Intraocular Pressure

Further Reading

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Prostanoids

- ▶ Prostaglandin Analogues

Prosthesis

- ▶ Ocular Prostheses

Proteinaceous Corneal Degeneration

- ▶ Keratinoid (Spheroidal) Degeneration
- ▶ Keratopathy Actinic (Labrador Keratopathy/ Spheroidal Degeneration)
- ▶ Spheroidal Degeneration

Pseudo Macular Hole

- ▶ Cellophane Maculopathy

Pseudoaccommodation

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Definition

Pseudoaccommodation is a name for optical phenomena which increase the depth of focus and can enable a presbyopic or pseudophakic eye to see in more than one distance without real accommodation, i. e., without a dynamic change in the dioptric power of the eye. Among these optical effects are pupillary constriction, bi- and multifocality, caused e.g., by a multifocal intraocular lens, astigmatism, or higher-order optical aberrations.

Cross-References

- ▶ Accommodation, Cataract
- ▶ Astigmatism
- ▶ Intraocular Lens
- ▶ Lens Capsule
- ▶ Presbyopia

Pseudoadenomatous Hyperplasia

- ▶ Sebaceous Hyperplasia of Eyelid

Pseudo-Best (Disease)

- ▶ Adult-Onset Foveomacular Vitelliform Dystrophy

Pseudoepitheliomatous Hyperplasia

- ▶ Papillomas, Eyelid

Pseudoexfoliatio lentis

- ▶ Pseudoexfoliation Syndrome

Pseudoexfoliation Syndrome

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Synonyms

PEX; *Pseudoexfoliatio lentis*; PXF

Definition

Elastic microfibrillopathy as an ocular manifestation of a systemic disorder is characterized by the deposition of whitish material on and within the structures of the anterior eye segment and is

frequently associated with severe chronic secondary open-angle glaucoma and cataract.

Histology

The hallmark of PEX syndrome is a pathologic production and accumulation of an abnormal fibrillar extracellular material in the anterior segment tissues. The characteristic PEX fibrils appear to be multifocally produced by various intraocular cell types including the preequatorial lens epithelium, nonpigmented ciliary epithelium, trabecular endothelium, corneal endothelium, vascular endothelial cells, and virtually all cell types of the iris (Naumann et al. 1998). Accordingly, clinical-histopathologic correlations focus on the involvement of the lens, the zonular apparatus, the ciliary body, the iris, the trabecular meshwork, and the cornea.

Immunohistochemistry

Immunohistochemistry shows that zonular disintegration may be facilitated by proteolytic mechanisms of lysosomal enzymes, particularly cathepsin B and metalloproteinases, within the PEX material.

Electron Microscopy

Scanning electron micrograph shows an accumulation of PEX material on the ciliary processes and the zonular fibers in the region of the pars plicata **and** loosened zonular lamella on the anterior lens capsule by accumulation of PEX aggregates. Transmission electron micrograph shows separation of the zonular lamella from the capsular surface by PEX material produced by the lens epithelium and erupting through the capsular surface and rupture of zonular lamella at sites of PEX material infiltration. Electron microscopy of the trabecular meshwork shows that the main deposition of PEX material appears to occur in the juxtacanalicular tissue adjacent to Schlemm's canal. Progressive accumulation of PEX material leads to a swelling of the juxtacanalicular tissue and a marked disorganization of Schlemm's canal architecture (e.g., narrowing of the canal lumen, collapse of the inner and outer walls, disruption of its endothelial lining, fragmentation into smaller channels, and partial obliteration by PEX material and degenerating endothelial cells) in advanced stages (Schlötzer-Schrehardt and Naumann 2006).

Molecular Diagnosis

PEX has a strong familial association. Single nucleotide polymorphisms (SNPs) in exon 1 of the lysyl oxidase-like 1 (LOXL1) gene have been identified as strong genetic risk factors for PEX syndrome and PEX glaucoma. LOXL1 is a pivotal cross-linking enzyme in extracellular matrix metabolism and seems to be required for elastic fiber formation and stabilization. Available data suggest that LOXL1 is differentially regulated dependent on the phase of progression of the fibrotic process. While increased levels of LOXL1 participate in the formation of abnormal PEX fiber aggregates in the initial phase of fibrogenesis, inadequate tissue levels may promote elastotic processes in advanced stages of the disease (Schlötzer-Schrehardt 2009).

Differential Diagnosis

- Pigment dispersion syndrome (PDS) is more often clinically bilateral and more common in young myopic males. PDS displays characteristic peripupillary iris transillumination defects and pigmentation of the chamber angle (Yanoff and Duker 2009).
- Capsular delamination (true exfoliation) is a rare condition that shows splitting of the anterior lens capsule without any deposition of fibrillary material. It may occur after heat exposure, trauma, irradiation, or inflammation (Yanoff and Duker 2009).
- Primary familial amyloidosis is a rare systemic disease with an abnormal deposition of a particular protein, called amyloid, in various

tissues of the body. In the anterior chamber, the disease displays white flocculent material in the pupillary margin and flaky substance on the surface of the lens (Yanoff and Duker 2009).

Cross-References

- ▶ Capsular Bag
- ▶ Familial Amyloidosis, Finnish Type
- ▶ Glaucoma Associated with Pigment Dispersion Syndrome (PDS)

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Pseudoexfoliative Glaucoma

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Synonyms

Exfoliative glaucoma

Definition

Secondary open-angle glaucoma associated with pseudoexfoliation (PEX) syndrome, a generalized disorder of the extracellular matrix. PEX syndrome has been characterized as a specific elastosis associated with the production and deposition of abnormal fibrillar PEX material deposits within intra- and extraocular tissues.

Etiology

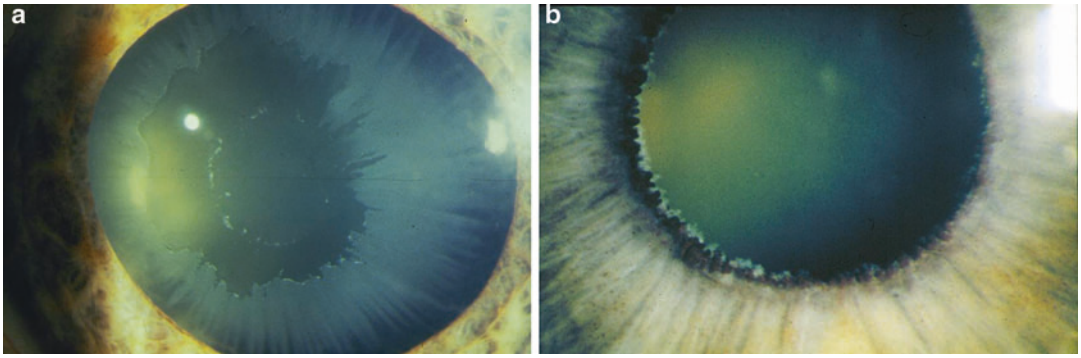
The underlying condition, PEX syndrome, represents a complex, multifactorial, late-onset disease of worldwide significance involving both genetic and nongenetic factors in its etiopathogenesis. Single nucleotide polymorphisms in exon 1 of the lysyl oxidase-like 1 *(LOXL1)* gene, coding for a cross-linking enzyme, have been identified as principal genetic risk factors for PEX syndrome/glaucoma. External factors including oxidative stress, hypoxia, low-grade inflammatory processes, and pro-fibrotic growth factors may act as co-modulating factors.

Clinical Presentation

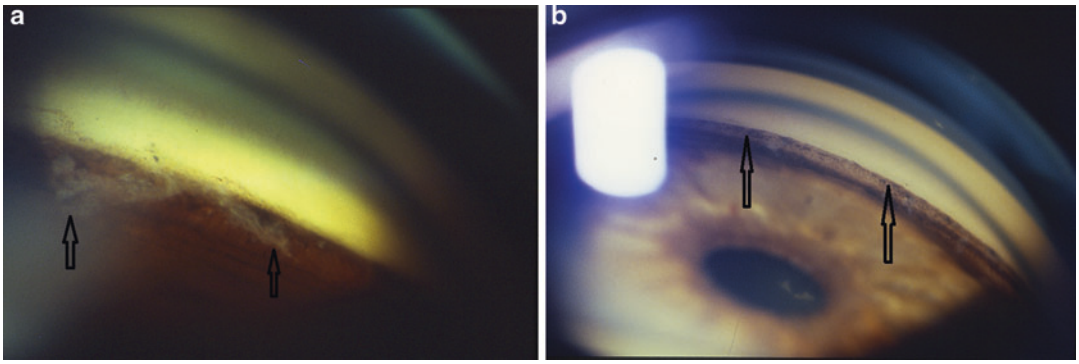
PEX glaucoma typically represents a high-pressure open-angle glaucoma with asymmetric presentation and pronounced chamber angle pigmentation. It is associated with high mean intraocular pressure levels, great diurnal pressure fluctuations and spikes, and rapid rates of progression. Pigment dispersion from the iris pigment epithelium may cause acute pressure rises after pupillary dilation. Narrowed chamber angles and smaller anterior chamber volumes due to a slight anterior movement of the lens may also induce angle-closure glaucoma via a pupillary block mechanism.

Diagnosis

Whitish flake-like deposits of PEX material can be observed on anterior segment structures, particularly on the anterior lens surface and the pupillary margin, occasionally also on the posterior surface of the cornea and on intraocular lens implants, as well as in the chamber angle by gonioscopy. The characteristic target-shaped



Pseudoexfoliative Glaucoma, Fig. 1 Clinical appearance of pseudoexfoliation syndrome. (**a**) Characteristic target-shaped pattern of PEX deposits on the anterior lens surface after pupillary dilation. (**b**) PEX material at the pupillary border



Pseudoexfoliative Glaucoma, Fig. 2 Typical appearance of the chamber angle as viewed by gonioscopy. (**a**) Accumulation of flakes of PEX material (*arrows*). (**b**) Irregular pigmentation (*arrows*) of the trabecular meshwork

pattern of PEX material accumulation on the lens can be only seen after pupillary dilation. PEX material deposition is usually accompanied by ancillary clinical signs, including pigment dispersion, peripupillary atrophy and pupillary ruff defects, pigment deposition on iris sphincter region, corneal endothelium, and trabecular meshwork as well as phacodonesis, iris hemorrhages, posterior synechiae, and insufficient pupillary dilation, particularly if asymmetrically present (Figs. 1 and 2).

Differential Diagnosis

Differential diagnosis of PEX syndrome/glaucoma includes true exfoliation of the lens, pigment dispersion syndrome and pigmentary glaucoma, and primary open-angle glaucoma.

Prophylaxis

Frequent consumption of fruit and vegetables was associated with a reduced risk of PEX syndrome in the Reykjavik eye study, suggesting that antioxidants may be protective against PEX syndrome/glaucoma.

Therapy

Since intraocular pressure is the main risk factor for progression, rigorous reduction and stabilization of

mean and diurnal 24-h intraocular pressure by means of medical, laser, or surgical therapy are crucial. A target IOP of <17 mmHg and lower was shown to prevent or slow progressive damage.

Prognosis

The prognosis of PEX glaucoma is more severe than that of primary open-angle glaucoma. There are greater 24-h pressure fluctuation, greater visual field loss and optic disk damage at the time of detection, poorer response to medications, more rapid progression, greater need for surgical intervention, and greater proportion of blindness.

Epidemiology

PEX syndrome occurs in all geographic regions worldwide with reported prevalence rates averaging about 10–20% of the general population over age 60. In all populations, the frequency rises with increasing age, with its incidence doubling every decade after the age of 50. PEX glaucoma accounts for approximately 20–25% of all open-angle glaucomas.

Cross-References

- ▶ Pigmentary Glaucoma
- ▶ Primary Open-Angle Glaucoma

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Pseudoguttatae

▶ Pseudoguttatae: Inflammatory Disease

Pseudoguttatae: Inflammatory Disease

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Synonyms

Inflammatory pseudoguttatae; Pseudoguttatae

Definition

Transient, reversible endothelial edema that looks clinically identical to the guttatae classically associated with Fuchs endothelial dystrophy (Zantos and Holden 1981).

Etiology

When inflammatory pseudoguttatae occur, they are typically noticed within hours to days from the onset of anterior segment inflammation. The most common causes include infectious keratitis, iritis, toxins, and thermokeratoplasty, though it has also been described in cases of viral conjunctivitis, trauma, and tight-fitting contact lenses (Zantos and Holden 1977).

Clinical Presentation

Inflammatory pseudoguttatae are visible under direct illumination as regions of focal thickening representing endothelial edema (Krachmer et al. 2011). In specular reflection, these areas appear as enlarged darkened patches with irregular contours against a hyperreflective endothelial mosaic (Nakashima et al. 2007). On occasion fine dustlike particles over the posterior surface of the endothelium can be seen.

Diagnosis

Typically pseudoguttatae can be diagnosed with serial simple slit-lamp examination confirming resolution of endothelial edema after appropriate management of the anterior segment disease. However, specular microscopy can also be useful for confirmation. Specular microscopy can demonstrate enlarged black patches (both discrete and confluent) within the endothelial mosaic. Endothelial cell counts obtained using this technique after the disappearance of pseudoguttatae show no difference from before the onset.

Differential Diagnosis

Transient endothelial blebs consist of increased separation between endothelial cells and circumscribed black zones obscuring the endothelial mosaic which form within minutes of contact lens insertion and resolve within an hour.

Guttatae are excrescences within the Descemet's membrane associated with adjacent endothelial dysfunction or loss. It is the hallmark of Fuchs endothelial dystrophy and are both progressive and irreversible, ultimately leading to stromal edema.

Chandler's syndrome, one of the three manifestations of iridocorneal endothelial (ICE) syndrome, may possibly be confused with corneal guttatae given the beaten-bronze appearance of the endothelium and associated corneal edema; however the endothelial changes are much finer in quality. It also is most common unilaterally, which would mimic pseudoguttatae more than the endothelial dystrophies. This condition, however, is more likely to occur in women, and intraocular pressure tends to be higher due to obstruction of the trabecular meshwork.

Herpetic disciform keratitis often presents with focal endothelial changes appreciable in specular reflection at the slit lamp; however keratic precipitates are often present in the area involvement; in pseudoguttatae, fine endothelial dusting can be seen, but keratic precipitates are not present. Additionally corneal edema is usually much more severe, requiring administration of topical steroids concurrent with antiviral medication.

Prophylaxis

Unclear

Therapy

Pseudoguttatae are treated by addressing the primary cause of inflammation.

Prognosis

Inflammatory pseudoguttatae have an excellent prognosis once the inflammation causing it has resolved.

Epidemiology

Unlike true guttatae which are more commonly seen in women, the limited data from the literature suggests there is no sex-related difference in the incidence of pseudoguttatae. As contact lens-related keratitis has been described as one of the leading causes of pseudoguttatae, the age at which pseudoguttatae is seen is typically much younger than in Fuchs endothelial dystrophy.

Cross-References

- ▶ Corneal Guttata
- ▶ Fuchs Endothelial Corneal Dystrophy (FECD)

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Pseudo-Hurler Polydystrophy

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Disease

Pseudo-Hurler polydystrophy, also known as mucolipidosis III (ML III), is a lysosomal storage disease resulting from a deficiency of the enzyme UDP-*N*-acetyl glucosamine *L*-phosphate transferase (C1cNAcPT) (Chen 2006). Symptoms usually appear at 3–5 years of age and are less severe and progress slower than Hurler syndrome. Non-ophthalmic features include no or mild mental retardation, skeletal abnormalities, coarse facial features, and short height (Yannuzzi 2010). Ophthalmic manifestations include corneal clouding, optic nerve head swelling, maculopathy, and retinal vascular tortuosity. Patients often survive beyond the fifth to sixth decade of life (Chen 2006).

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Pseudo-Hypertelorism

- ▶ Telecanthus

Pseudomembrane, Conjunctival

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Synonyms

Pseudomembranous conjunctivitis

Definition

Pseudomembrane is composed of gray fibrin and inflammatory material and is avascular. Pseudomembranes can be peeled without bleeding due to their deposition on an intact conjunctival epithelium and lack of vascularity, in contrast to true membranes which contain highly concentrated fibrin deposited within conjunctival epithelium and stroma. These are most commonly seen in viral infections, including adenovirus and herpes viruses. However, potential etiologies include bacterial infections such as beta-hemolytic streptococcus, fungal infections including *Candida albicans*, chemical burns, and immunological diseases including ligneous conjunctivitis.

Cross-References

- ▶ Adenoviral Keratoconjunctivitis
- ▶ Ligneous Conjunctivitis

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Pseudomembranous Conjunctivitis

▶ Adenoviral Keratoconjunctivitis
▶ Pseudomembrane, Conjunctival

Pseudoneuritis

▶ Pseudopapilledema
▶ Pseudopapilledema: Disc Drusen

Pseudopapilledema

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Synonyms

Congenitally anomalous disk; Pseudoneuritis

Definition

Normal variant elevation of the optic disk, disk drusen, disk abnormalities, or congenital fullness of the optic nerve without vessel leakage or optic disk edema can mimic papilledema and is referred to as pseudopapilledema.

Etiology

Pseudopapilledema is a familial condition that can be caused by a congenitally narrow scleral canal, myelinated fibers, anomalous disks, or optic disk drusen. Pseudopapilledema in contrast to true papilledema is not caused by elevation in intracranial pressure.

Clinical Presentation

Most patients with pseudopapilledema will not report any visual or systemic symptoms, although visual field defects (e.g., nerve fiber layer defects, enlarged blind spot) are detectable upon examination.

Diagnostics

Pseudopapilledema is sometimes difficult to differentiate from true papilledema (a true swelling of the optic disk). Typically, ophthalmoscopic analysis will reveal a normal color to the optic disk (e.g., yellow or yellowish pink) with blurred margins but no obscuration of the retinal nerve fiber layer from true edema and no obligatory signs of increased intracranial pressure. Optic disk drusen (hyaline bodies) either visible or buried may be present. Hemorrhage is not usually present in pseudopapilledema but if present will be of the subretinal, retinal, or vitreous variety (rather than the splinter hemorrhages seen in true papilledema). The peripapillary retinal nerve fiber layer typically appears clear without obscuration of the underlying retinal blood vessels as they cross the disk margin. There is usually an absence of cupping of the optic disk in pseudopapilledema from disk drusen or anomalous disks. The condition can be unilateral (one-third of patients) or bilateral and may be asymmetric. Fluorescein angiography will show no vessel leakage of dye unlike in true papilledema. A spontaneous venous pulse may be present but may be absent in up to 20% of normal individuals.

Differential Diagnosis

True papilledema, optic disk drusen, vitreopapillary traction, hypertropia, myelinated nerve fiber, and optic nerve hypoplasia.

Prophylaxis and Therapy

There is no prophylaxis or therapy for pseudopapilledema.

Prognosis

Although pseudopapilledema has been associated with nerve fiber layer-type visual field defects, there is typically no decrease in visual acuity because the papillomacular bundle is not usually affected by pseudopapilledema (e.g., disk drusen). If however macular hemorrhage or choroidal neovascular membrane occurs, central visual loss may result. In pseudopapilledema with the presence of optic disk drusen, visual field defects may slowly progress with age, but most patients are usually only modestly affected or are asymptomatic.

Epidemiology

Pseudopapilledema with optic disk drusen is present in approximately 2% of the general population and is more common among Caucasians compared to those of African American descent.

Cross-References

► Diabetic Disc Edema
► Optic Nerve Head Drusen

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Pseudopapilledema: Disc Drusen

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Synonyms

Buried disc drusen; Disc hyaline bodies; Pseudoneuritis; Pseudopapilledma

Definition

Optic disc drusen (ODD) are congenital or developmental optic disc abnormalities that tend to become more noticeable and superficial by

ophthalmoscopy over time. These yellowish depositions have a "globular lumpy-bumpy" appearance on and around optic nerve head distorting the edges of optic disc and producing an anomalous, elevated appearance with loss of the physiologic optic cup and may be mistaken for true disc edema. ODD are mostly asymptomatic and can be an incidental finding during routine eye examination. It is important to evaluate patients with ODD and appropriately document the findings in order to avoid unnecessary neurological testing as it can be misdiagnosed true disc edema later. There is no proven treatment for ODD but many patients even with abnormal visual fields remain asymptomatic.

Etiology

ODD is believed to be an abnormal accumulation of protein and calcium salts in the optic disc due to disturbances in axonal metabolism in the presence of small scleral canal. ODD are composed of mucopolysaccharides, amino acids, ribonucleic and deoxyribonucleic acid, calcium, and iron.

Epidemiology

The incidence of ODD is 3.4–24 per 1000 in general population. Bilateral ODD had been reported in approximately 75–85% but ODD can be markedly asymmetric or even strictly unilateral. They are more common in Caucasians. Most cases are sporadic but an inheritance pattern when present is often autosomal dominant pattern with incomplete penetrance. ODD is typically an isolated finding but may be associated with other conditions (e.g., pseudoxanthoma elasticum, angioid streaks, retinitis pigmentosa).

Clinical Presentation

Most patients with ODD are asymptomatic and many are incidentally found during routine eye examination in childhood. Some patients, however, may experience transient visual obscurations (TVOs) lasting seconds at a time and can be described as flickering or graying of vision as seen in true papilledema. Although nerve fiber layer visual field defects are common, central vision is usually preserved. Loss of visual acuity has been reported in cases with concomitant retinal vein occlusion, nonarteritic anterior ischemic optic neuropathy, or juxtapapillary choroidal neovascularization.

ODD produce an elevated optic disc and the presence of the visible superficial refractile yellow bodies in optic discs is usually diagnostic. Signs of true disc edema such as exudates, cotton wool patches, and flame hemorrhages are absent in ODD. In younger patients, ODD are often buried and are not obviously visible on the surface of the disc. As patients get older, however, increased calcium and protein accumulation occur and ODD move more superficially and can then be more easily observed on funduscopic examination.

Up to 70% of patients with ODD have visual field defects with the most common patterns being nonspecific enlargement of the blind spot, inferior or less commonly superior retinal nerve fiber layer defects, or generalized constriction, increased retinal vascular tortuosity, dilated veins, and abnormal branching with trifurcation, and crossing of horizontal midline by temporal branches of central retinal arteries have been documented in discs with ODD. There is also a reported increase in the incidence of cilioretinal arteries in up to 20–40% of ODD in contrast to the general population of 15%.

Diagnosis

Although most cases of ODD can be diagnosed by clinical exam alone, B-scan ultrasonography can be useful for the detection of ODD especially when buried. The classical finding of ODD on B-scan ultrasonography is a highly reflective round structure in the optic disc head with acoustic shadowing. Due to their high concentration of calcium, the hyperechoic lesion can still be

detected even with a low-gain scan. B-scan is the most sensitive method to detect ODD which are calcified but do not have good sensitivity for noncalcified ODD (Atta 1988; Kurz-Levin and Landau 1999).

Although computed tomography (CT) scan is almost as sensitive as B-scan in detection of calcified ODD, ultrasound is cheaper, easier to perform, and has better resolution. In addition, exposure to radiation and the higher cost associated with CT scan make B-scan ultrasonography a more suitable method for routine diagnosis of ODD. We do not typically image ODD but patients with central visual loss, progressive and rapid visual defects, non-nerve fiber layer defects (e.g., homonymous or bitemporal hemianopsia), concomitant optic disc edema, or optic atrophy might benefit from further evaluation including neuroimaging as ODD does not protect one from the development of alternative etiologies for visual loss.

ODD may exhibit autofluorescence on the pre-injection fluorescein angiogram. Fundus fluorescein angiography (FFA) can also be used to help differentiate difficult cases of ODD from true papilledema, as disc leakage occurs in true disc edema versus late staining in ODD. Optical coherence tomography (OCT) is a newer noninvasive optical technique for ODD. The advantage of OCT is the ability to detect concomitant RNFL loss with high reproducibility. The nasal RNFL tends to be the first quadrant to be affected in ODD. Newer generation OCT can also show the underlying ODD ("boot sign") but it remains to be seen if OCT will replace FFA and B-scan ultrasonography in differentiating true disc edema from ODD.

Differential Diagnosis

1. Papilledema
2. True optic disc edema secondary to other causes (e.g., inflammatory, infectious, ischemic, hereditary etc.)

Therapy

There are no proven treatment modalities for ODD. In presence of visual field defect, routine tonometry and visual field tests are reasonable as well as baseline photos or OCT. Antiglaucomatous therapy in selected cases can be considered if there is clear evidence of elevated or borderline intracranial pressure elevation or in cases of severe RNFL loss. The clinical challenge lies in determining if the RNFL loss is due to glaucomatous damage or ODD alone. In small and congested optic disc, it is difficult to determine glaucomatous cupping since it is masked by crowding of optic nerve head. Furthermore, the visual field defects secondary to ODD mimic those of glaucoma (Auw-Haedrich et al. 2002). It has been our practice to consider IOP lowering agents in patients with ODD who are glaucoma suspects.

Prophylaxis

Nonapplicable.

Prognosis

Patients with ODD typically have mild or no symptomatic vision loss. In one study, the average vision loss rate was about 1.2% per year (Lee and Zimmerman 2005).

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Pseudopapilledma

▶ Pseudopapilledema: Disc Drusen

Pseudoproptosis

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Definition

Pseudoproptosis is the simulation of abnormal prominence or a true asymmetry that is not associated with displacement of the globe.

Etiology

Causes of pseudoproptosis result from asymmetries of the bony orbit, globe, and eyelid including:

Enlarged globe (high myopia, buphthalmos)
Contralateral enophthalmos (contralateral enophthalmos, contralateral small globe, contralateral cicatricial tumor)
Asymmetric orbital size (congenital, post-irradiation, postsurgical)
Asymmetric palpebral fissures (ipsilateral eyelid retraction, scarring or facial nerve paralysis, or contralateral ptosis)

Occurrence

Pseudoproptosis is most commonly seen in eyelid retraction, high myopia, and contralateral enophthalmos. Eyelid retraction, which is associated with thyroid eye disease, produces a more prominent appearing eye and can coexist with true proptosis. Unilateral high axial myopia can mimic proptosis owing to the increased length of the myopic eye. Acute enophthalmos, often secondary to orbital blow-out fracture, may cause apparent proptosis of the contralateral eye. However, the diagnosis of pseudoproptosis should not be made until the possibility of a mass lesion has been ruled out.

Classification

Pseudoproptosis can be classified into three broad categories including abnormalities of the globe (asymmetric myopia, buphthalmos), altered lid position (ptosis, lid retraction, surgical recession of the muscles, third nerve palsy), and structural lesions (facial asymmetry, contralateral enophthalmos, posttraumatic disorders).

Cross-References

▶ Graves' Disease
▶ Proptosis

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Pseudoptosis

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Synonyms

Functional ptosis; Nonorganic ptosis

Definition

Pseudoptosis is apparent but not true drooping of the eyelid (see ptosis). Pseudoptosis is typically unrelated to neurological or musculoskeletal defects of the eyelid.

Etiology

Pseudoptosis may be the result of abnormal size of the eye such as the absence of eye development (anophthalmos); a shrunken, non-functional eye (e.g., phthisis bulbi); a small eye (microphthalmos); and posterior placement of the eyeball (enophthalmos), which all present as apparent ptosis without defect to the eyelid mechanisms themselves. Abnormal growth or placement of eyelid tissue such as excessive loose skin of the eyelid (dermatochalasis), contralateral retraction of the eyelid, or prolapse of orbital fat (blepharochalasis) might also result in the pseudoptosis. Bulging of one eye (proptosis) or lid retraction due to thyroid eye disease may result in the diagnosis of possible ptosis in the contralateral eye when in reality it is pseudoptosis. Similarly, an eye with a hypotropia might also result in pseudoptosis. When the patient attempts to fixate on objects with the hypertropic eye, the contralateral eye (the hypotropic eye) might appear to have ptosis. Patients who are unable to infraduct (e.g., downgaze paralysis) might also exhibit bilateral pseudoptosis.

Narrowing of the eyelid fissure due to unilateral facial spasms (hemifacial spasm) or eyelid spasms (blepharospasm) may also give the appearance of ptosis. Overactivity of the orbicularis oculi muscles is also common and is usually proportional to the amount of eyelid fissure narrowing and eyebrow depression from frontalis muscle inactivity.

Pseudoptosis has also been observed in conversion disorder (psychogenic pseudoptosis), revealed by normal pathology findings and positive effect with a placebo.

Clinical Presentation

Pseudoptosis presents as ptosis without defects related to eyelid position. It may be secondary to one of the following primary manifestations: anophthalmos, microphthalmos, enophthalmos, phthisis bulbi, dermatochalasis, blepharochalasis, facial spasms from narrowing of the eyelid, lid retraction of the contralateral eye, or chronic Bell's palsy.

History

At the beginning of the twentieth century, there was considerable debate about the presence of functional weakness in the face as part of "hysteria" (modern day conversion disorder). For example, in 1889, Charcot stated that out of the many cases he had seen of functional limb weakness as a result of hysteria, the face remained absent of that weakness; however, Janet in 1907 claimed to have seen numerous cases of "hysterical facial paralysis." Janet's early descriptions likely included functional facial weakness of the eyelid, which is known today as psychogenic pseudoptosis. Today it is known that pseudoptosis can have other causes such as dermatochalasis and blepharochalasis.

Diagnosis

In order to distinguish pseudoptosis from organic ptosis, appropriate facial muscle movements should be examined for hemifacial spasm or blepharospasm. Characteristically, pseudoptosis patients with orbicularis spasm have a depressed eyebrow with variable ability to elevate the frontalis muscle, compared to organic ptosis patients who generally exhibit frontalis muscle overactivity to compensate for true ptosis. Patients should also undergo evaluation for proptosis, ocular misalignment (e.g., hypertropia), contralateral eyelid retraction, or mechanical causes (e.g., dermatochalasis) for pseudoptosis.

Differential Diagnosis

Ptosis, anophthalmos, microphthalmos, enophthalmos, phthisis bulbi, dermatochalasis, blepharochalasis, and Bell's palsy.

Treatment

Treatment should be directed at the etiology of the pseudoptosis, for example, botulinum toxin injections for lid spasm, treatment of lid retraction or proptosis in thyroid eye disease, or treatment of ocular misalignment in strabismus. In some cases positive reinforcement or psychologic therapy is sufficient for cases of psychogenic pseudoptosis.

Prognosis

Full recovery is expected for most patients depending on treatment of the underlying etiology. In the case of psychogenic disorders, spontaneous resolution may occur with positive assurance, but some cases have also shown continuation of psychogenic pseudoptosis for a few years following initial diagnosis.

Epidemiology

The frequency of organic ptosis has not been officially reported in the United States or worldwide. As a result, the frequency of pseudoptosis is also unknown.

Cross-References

- ▶ Bell's Palsy
- ▶ Functional Ptosis

Further Reading

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Pseudotumor Cerebri

► Idiopathic Intracranial Hypertension

Pseudo-Vitelliform (Macular Dystrophy)

► Adult-Onset Foveomacular Vitelliform Dystrophy

Psychedelic Drug

► Drugs: Hallucinations

Psychogenic

► Nonorganic Visual Loss

Psychogenic Micropsia

► Micropsia

Pterygium

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Definition

A fibrovascular growth of conjunctiva that extends from the bulbar region of the conjunctiva onto the cornea

Etiology

Pterygia are not well understood and the pathogenesis is mostly unknown (Tan and Chan 2011). However, many studies have shown that UV exposure is a risk factor for pterygium (Chow et al. 2009; Tan and Chan 2011). This may produce a limbal stem cell dysfunction and deficiency due to the UV exposure, which shows the typical pterygium characteristics of fibrovascular growth and inflammation (Tan and Chan 2011). Historically, pterygia were described as a degenerative disorder, but current opinion labels pterygia as a proliferative growth disorder (Tan and Chan 2011). Pterygia's high propensity for recurrence and the similar treatment to that of anti-cancer therapy support this classification (Tan and Chan 2011).

There are changes in the pterygium cells that make them behave differently. Pterygium fibroblasts respond to TGF-beta differently than normal fibroblasts and may play a role in pathogenesis (Tan and Chan 2011). They also have increased levels of matrix metalloproteinases and greater levels of bFGF and IGF-II, which may contribute to this altered response (Tan and Chan 2011).

Clinical Presentation

Pterygia grow gradually and typically present in an individual's 20s to 40s (Chow et al. 2009). The name refers to the characteristic winglike growth, and the morphology of the fibrovascular growth is divided into the head, neck, and body (Coroneo and Chui 2013). The head is attached to the cornea and extends onto the cornea and includes a white avascular cap. The neck is a narrowed portion of tissue extending from the bulbar region of the eye to the peripheral cornea. The body is the thicker tissue that lies on the sclera and is continuous with the conjunctiva (Chow et al. 2009; Coroneo and Chui 2013). The pterygium can appear as low-grade avascular pterygium or as high-grade fleshy pterygium. They also may show iron lines near the pterygium head called a Stocker line (Coroneo and Chui 2013).

A pterygium typically appears nasally, but can arise temporally too (Chow et al. 2009). They present unilaterally or bilaterally, and in some cases of double pterygium, one eye can have a nasal and a temporal pterygium (Chow et al. 2009).

Pterygium may cause significant irritation and foreign body sensation due to the irregular shape or dry eye symptoms induced (Rich 2008; Tan and Chan 2011). It often produces a with-the-rule astigmatism and in advanced cases can grow far enough onto the cornea to obstruct vision (Tan and Chan 2011; Coroneo and Chui 2013). They also can advance enough to restrict ocular motility.

Diagnostics (Lab Diagnostics)

Pterygia have a characteristic appearance, and clinical observation alone is often sufficient to make a diagnosis. In cases with uncertainty, an excisional biopsy is appropriate.

Differential Diagnosis

- Pinguecula – Unlike pterygium, these do not invade the cornea.
- Pseudopterygium – These arise from trauma or chemical insult and do not adhere to the limbus (Chow et al. 2009).
- Conjunctival tumors including papilloma, lymphoma of the conjunctiva, nonpigmented nevi, squamous cell carcinoma, and melanoma
- Leukoplakia

Prophylaxis

The major prevention of pterygium is the reduction of UV exposure, especially for outdoor workers. Sunglasses, glasses, and hats have proven to reduce the incidence of pterygium (Rich 2008; Chow et al. 2009; Coroneo and Chui 2013). Other preventable risk factors like smoking and alcohol use remain controversial in their preventative or incidence role (Chow et al. 2009).

Therapy

Therapy can begin in the early stages of the disease and include lubricating drops and when needed steroid and vasoconstrictive drops (Rich 2008; Coroneo and Chui 2013). These can alleviate symptoms, but do not prevent progression.

In cases with significant irritation, astigmatism, obstruction of visual acuity, or loss of ocular motility, surgical intervention is recommended (Chow et al. 2009). Also, in cases of cosmesis, the patient may elect to have pterygium excision. Surgical management includes many types of surgical procedures and adjuvants, but there is no consensus on the best procedure. Surgeons must evaluate each case by the resources available, the risk of recurrence, and the safety. The procedures include bare sclera, simple conjunctival closure, conjunctival autografting, and amniotic membrane grafting. These procedures can be done under local anesthesia, but in the more complicated techniques, a peribulbar or retrobulbar anesthesia is recommended (Rich 2008; Chow et al. 2009). In procedures utilizing grafts, sutures or fibrin glue can serve as attachment methods. Additionally, adjunctive medical therapies of beta-irradiation, mitomycin C, or 5-fluorouracil can supplement the procedure.

Bare sclera was the first technique developed and involves excising the pterygium and leaving the sclera bare to epithelize on its own. It is a quick and simple procedure, but alone is not recommended due to its high recurrence rates ranging 24–89% (Tan and Chan 2011). With any of the procedures excising the pterygium, some surgeons will use a technique to balloon the conjunctiva with fluid before excision (Chow et al. 2009).

Another simple and quick procedure is the simple conjunctival closure after pterygium excision. This technique uses sutures to apposition the conjunctiva superior and inferior to the defect and closes them over the sclera. While not well studied, unfavorable recurrence rates of 29% and 37% have diminished its use (Tan and Chan 2011).

The conjunctival autograft is a popular procedure. It uses a donor graft taken from bulbar conjunctiva, typically in the superior portion of

the patient's eye, to cover the defect made after pterygium excision. It benefits from low complications, low recurrence, and excellent cosmesis (Chow et al. 2009; Coroneo and Chui 2013). The procedure's drawbacks are greater technical demands, longer operation times, and more patient pain (Chow et al. 2009). A related procedure, the conjunctival limbal autograft, extends the donor graft into the limbus to transfer limbal stem cells. This is believed to restore anatomical function and relieve the local stem cell deficiency (Chow et al. 2009). It also has low recurrence rates, but debate exists to whether it improves outcomes compared to the less complicated conjunctival autograft. Both kinds of autografts have historically been attached to the sclera using sutures, and these produce excellent outcomes. Recent studies have shown that fibrin glue is a competitive alternative that provides quicker surgical times, less postoperative discomfort, and, in many studies, lower recurrence rates (Chow et al. 2009; Tan and Chan 2011; Coroneo and Chui 2013).

The amniotic membrane graft is another promising procedure with good outcomes and low recurrence rates. Amniotic membranes are available frozen or dried and have anti-inflammatory and antifibroblast properties (Chow et al. 2009). Additionally, it matches the conjunctiva's alpha-subunit layout of collagen IV (Tan and Chan 2011). Some studies show higher recurrence rates than the conjunctival autograft, but still much better than bare sclera (Tan and Chan 2011). The amniotic membrane graft is most useful in sparing the conjunctiva for other procedures that may be needed like glaucoma surgery. Also in large pterygia requiring large grafts, an amniotic membrane can be used. Some patients with scarred conjunctiva or insufficient remaining conjunctiva from multiple recurrent pterygium may also benefit from the amniotic membrane transplant (Rich 2008; Tan and Chan 2011).

Complications of surgery are generally not severe or vision threatening. Conjunctival autografts may have graft edema, hemorrhage, retraction, necrosis, or dellen formation (Tan and Chan 2011). Intraoperative complications can include perforation of the sclera or cornea and excessive bleeding (Chow et al. 2009). With the grafts, the graft may become flipped from the anatomical orientation. Postoperatively, graft dehiscence, granulomas, symblepharon, and inclusion cysts can arise (Chow et al. 2009).

In addition to surgery, adjunctive medical therapy can also lower the rates of recurrence. Beta-irradiation from strontium-90 has been used for a long time and can lower recurrence (Rich 2008). Dosing is typically 1000–3000 rad doses in single or fractionated doses (Chow et al. 2009). The recurrence rates after beta-irradiation are in the 10% range, but the technique is not well studied (Chow et al. 2009; Tan and Chan 2011). However, serious complications with some latency periods of greater than 10 years do occur and include scleral and corneal necrosis, corneal ulceration, symblepharon, iritis cataract, infectious scleritis, and secondary glaucoma (Rich 2008; Chow et al. 2009; Tan and Chan 2011).

5- 5-Fluorouracil is another adjunctive therapy and works by inhibiting DNA synthesis. Intraoperative use has shown to lower recurrence to 10–20%, but more studies are needed on its effects (Chow et al. 2009).

Mitomycin C is a popular adjunctive treatment for many procedures. This adjuvant works by inhibiting DNA, RNA, and protein synthesis, and it is most effective on rapidly growing cells (Chow et al. 2009; Tan and Chan 2011). Mitomycin C lowers the recurrence rates of each procedure compared to without mitomycin C and can be administered preoperatively, intraoperatively, or postoperatively (Chow et al. 2009). Recurrence rates are roughly less than 10% for primary cases and 20% for recurrent cases (Chow et al. 2009). The earliest use was in postoperative drop regimens typically lasting 4–14 days with 0.2–0.4 mg/mL drops 2–4 times daily (Chow et al. 2009). The use of mitomycin C does have risks of scleral melting, corneal edema, necrotizing scleritis, corneal and scleral perforation, sudden onset mature cataract, photophobia, and secondary glaucoma, and the reports of these vision threatening complications are highest in postoperative drop regimens (Chow et al. 2009; Tan and Chan 2011). Intraoperative use is more favored today and dosed in 0.2–0.4 mg/mL for

2–5 min once the pterygium has been excised (Chow et al. 2009). It is widely used, but it should be used judiciously in knowledge of the known complications and possible unknown long-term adverse affects.

Prognosis

A pterygium is gradually progressive. In some cases, a pterygium may be small and stable and will require no intervention. This is why photographing can be important in evaluating the changes of the pterygium. When surgical intervention is required, recurrence is the major outcome of interest. The rates of recurrence depend on the type of procedure, grade of pterygium, and patient history. Recurrence is highest in the bare sclera and simple conjunctival closure techniques, and the conjunctival autograft and amniotic membrane grafts have much lower recurrence rates (Chow et al. 2009; Tan and Chan 2011). These procedures can have their recurrence rates lowered through the use of adjunctive therapies like mitomycin C commonly, or 5-fluorouracil or beta-irradiation, but may carry additional side effects.

Recurrence is associated with higher-grade pterygium. The higher-grade fleshy pterygium recurs more often than the lower-grade atrophic pterygium (Rich 2008; Tan and Chan 2011). Additionally, patients with a history of recurrence are also more likely to recur than patients presenting with primary pterygium (Rich 2008).

The time to recurrence is typically within 6 months and almost all cases within 1 year (Chow et al. 2009). Pterygium that recur typically are more aggressive and larger than the previously excised pterygium (Tan and Chan 2011).

Epidemiology

Pterygium is found worldwide, but rates have been reported highest near the equator and tropical regions (Rich 2008; Coroneo and Chui 2013). There is a pterygium belt 37° above and below the equator where the highest prevalence is found (Tan and Chan 2011). The highest rates include the study in Barbados that found a prevalence rate of 23.7% in black individuals (Chow et al. 2009). That is in comparison to the study in Victoria, Australia, which found a prevalence rate of 1.2% in urban residents (Chow et al. 2009).

Pterygium prevalence is highest in older ages, but most importantly those with the greatest UV exposure (Coroneo and Chui 2013). Another factor, rural residence, is also associated with higher prevalence of pterygium, although this may be due to other factors associated with rural residence (Coroneo and Chui 2013). Controversy exists whether male gender, race, and smokers have higher prevalence rates (Chow et al. 2009). Genetics may also play a role in pterygium prevalence, but this is not strongly established.

Cross-References

- ▶ Conjunctival Degenerations
- ▶ Lymphoma: Definition
- ▶ Melanomas, Conjunctival
- ▶ Papilloma
- ▶ Pinguecula
- ▶ Squamous Cell Carcinoma of Eyelid

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Pubic Lice

- ▶ Phthirus Pubis (Crab/Pubic Louse), Ocular Infection

Pulsation, Orbital

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Synonyms

Orbital pain

Definition

Orbital pain can be caused by many different disorders of the orbit. Typically it is described as a deep, dull ache behind or in the eye.

Occurrence

Although orbital pain is not a feature of many orbital processes, it may be a significant and characteristic symptom of acute inflammation and infection. Pain may also be a feature of malignant tumors that have perineural spread.

Classification

Many different orbital diseases cause pain and can be broadly classified by etiology including infection, inflammation, hemorrhage, and neoplasm. This includes infection such as orbital cellulitis where pain is typically with extraocular movement. Acute inflammation such as orbital inflammatory syndrome and Tolosa-Hunt can also cause orbital pain, ophthalmoplegia, and decreased vision. In Wegener's granulomatosis, painful proptosis as well as reduced ocular motility is caused by necrotizing vasculitis and granulomatous inflammation. Retrobulbar hemorrhage may cause significant pain as well as optic nerve compression and is considered an ocular emergency. Most of the slow growing benign tumors typically do not cause significant pain. However, malignant tumors may cause orbital pain due to perineural spread such as adenoid cystic carcinoma of the lacrimal gland and invasion from adjacent nasopharyngeal carcinoma or metastatic lesions.

Cross-References

▶ Accessory Lacrimal Glands
▶ Orbital Cellulitis
▶ Orbit, Inflammation of

Further Reading

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Punctate Epithelial Defects

▶ Punctate Epithelial Defects/Erosions

Punctate Epithelial Defects/Erosions

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Synonyms

PEEs; Punctate epithelial defects

Definition

A breakdown of healthy corneal epithelium resulting in pinpoint defects with positive fluorescein, lissamine green, or rose bengal staining seen via a slit-lamp examination.

Etiology

Tear film instability, desiccation, or inflammatory changes of the cornea resulting in a breakdown of

the healthy epithelium. Causes include infectious, allergic, neurologic, toxic, or autoimmune diseases. Inflammation from these diseases leads to a secondary tear deficiency that may then lead to further epithelial disruption.

Occurrence

PEE is a nonspecific sign that occurs in many disease processes, usually as a result of instability of the tear film. The location and pattern of the PEE are important to determine the causative agent.

Classification

A full medical history should be conducted targeting autoimmune disorders, infiltrative processes, infectious causes, neuropathic disorders, and endocrine dysfunction. During examination, one of the aforementioned stains should be instilled into the eye. The location of the PEE will aid in the diagnosis. Diffuse PEE may be caused by viral conjunctivitis, early bacterial conjunctivitis. or medicamentosa. PEE across the lower one third of the cornea may be due to staphylococcal blepharoconjunctivitis, trichiasis, or eyelid malposition. PEEs confined to the intrapalpebral zone are usually related to drying of the cornea secondary to exposure. On the superior one third of the cornea, PEEs are generally related to superior limbic keratoconjunctivitis, vernal conjunctivitis, or floppy eyelid syndrome. Other patterns include vertical linear PEE from foreign bodies lodged underneath the lid and areas where inappropriately fitting contact lenses touch the cornea.

One must differentiate PEE from punctate epithelial keratitis (PEK) and superficial punctate keratopathy (SPK). PEK will have corneal infiltrates associated with the negative staining pattern and is thought to be a progression of the PEE to becoming subepithelial infiltrates (SEIs). SPKs generally have a negative staining pattern with associated positive staining apex and are found in Thygeson's keratopathy.

Cross-References

- ▶ Keratoconjunctivitis Sicca
- ▶ Tear Film (Tears)
- ▶ Thygeson's Superficial Punctate Keratopathy

Further Reading

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Punctate Inner Choroidopathy

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Introduction

Punctate inner choroidopathy is an uncommon posterior multifocal chorioretinopathy first described by (Watzke et al. 1984). It is characterized by the presence of small, focal, yellow lesions at the posterior pole occurring at the level of the inner choroid/retinal pigment epithelium in the absence of vitreous inflammation. It usually affects young, myopic females (who may also be fair haired with blue- or light-colored irides).

The usual presenting symptoms include blurred vision, scotomata, and/or photopsia. These usually occur due secondary to inflammatory foci at the time of presentation, but can be caused by choroidal neovascularization (CNV) complicating the inflammatory focus or by scarring consequent to the inflammation.

Despite having such a distinct clinical phenotype, there remains some controversy as to whether this disease simply represents part of a larger spectrum of chorioretinal disorders of unknown origin, including idiopathic multifocal

choroiditis (MFC), the white dot syndrome (WDS) spectrum, and idiopathic or myopia-associated CNV formation.

Although the majority of cases run a self-limited course, up to 69% of eyes may develop CNV, and furthermore about half of eyes develop subretinal fibrosis with consequent visual loss often characterized by enlarging and new scotomata and in some cases further impairment of vision.

Immunogenetics

There remains some speculation as to whether the WDS share a common immunopathogenic pathway, given their overlap in clinical phenotype, and a preceding infection as their trigger to an innate immune dysregulation (Jampol and Becker 2003). However, despite several studies having demonstrated an association between the HLA-B7 and DR2 haplotypes and patients with POHS, these findings have not been consistently reproduced in other types of chorioretinal disorders within the WDS. Nevertheless, the HLA-DR2 haplotype is more common in British patients with PIC compared to similar clinical phenotypes such as MFC with panuveitis. Genome-wide association studies have provided new insights into the genetics of uveitis and suggest that in most circumstances any inherited predisposition is likely to involve non-HLA genes. There is an association between the IL-10 gene and susceptibility to develop WDS, and some IL-10 haplotypes are more common in patients with PIC and MFC with panuveitis (Atan et al. 2011). In addition to this, dysregulation of the complement system, a key component of the innate immune system, has also been linked with the development of different immune-related disorders, including CNV proliferation, and a strong link between the Y402H allele and IVS1 in the CFH locus and MFC has been described.

Imaging

Traditionally, colour fundus photography has provided the gold standard for documenting and classifying the clinical phenotype of PIC lesions into typical (less than one quarter of the disk diameter, located within the arcades, and absent around the papillary margin) and atypical (more than one quarter of the disk diameter, outside the arcades, and including a peripapilly distribution). Furthermore, retinal photographs are still extensively used to monitor disease progression (Table 1).

More recently, optical coherence tomography (OCT) technology provides real-time, noninvasive imaging of retinal tissues. High-resolution SD-OCT demonstrates the presence of elevated lesions in the sub-RPE space and outer retina during the acute inflammatory phase. Serial imaging with SD-OCT demonstrates the progressive and uneven changes of choroid, RPE, and retinal lesions and allows for the monitoring of disease progression (Zhang et al. 2013) (Table 1).

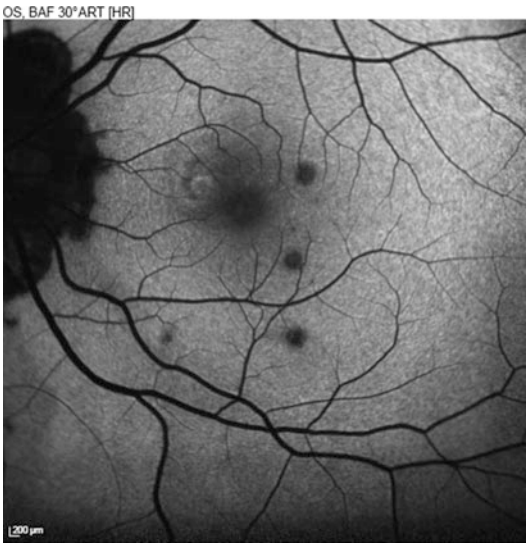
The use of enhanced depth image optical coherence tomography (EDI-OCT) provides high-resolution cross-sectional images of deeper regions in the eye, enabling the evaluation of inner choroidal thickness. Although this imaging modality may be of greatest use in inflammatory or vascular disorders with more diffuse choroidal involvement, it has shown a small increase of choroidal thickness beneath active PIC lesions. Furthermore, in patients with "presumed" quiescent disease, localized RPE elevation with underlying hyporeflectivity may be an early marker of subclinical activity (Spaide et al. 2013).

Accumulation of metabolic waste products from the outer segments of photoreceptors in the RPE can be visualized by means of fundus autofluorescence (FAF), allowing this technique to assist in the evaluation of the status of the photoreceptor-RPE complex. FAF has very low specificity for characterizing PIC lesions but can be useful in monitoring disease activity as hyperautofluorescence is not only as an indicator of disease activity, due to the displacement of lutein pigment, but is also associated with CNVM formation. In contrast, hypoautofluorescence may indicate RPE death/loss, as well as being an indicator of disease remission (Fig. 1).

Finally, angiography remains a very useful tool in order to detect subclinical lesions that are not

Punctate Inner Choroidopathy, Table 1 Clinical phenotypical stages of PIC with corresponding imaging findings

Stage	Fundus examination	FFA	ICG	SD-OCT
I	Normal	Normal	Blurring choroidal vessels and mild to moderate hypofluorescence spots	Slight irregularities in the outer nuclear layer
II	Normal or mild spot discoloration	Normal to mild window defect	Better demarcated hypofluorescence spot	Focal elevation of the RPE with corresponding inner/outer segment interface disruption
III	Yellow-cream spot with blurred margins	Early hyperfluorescent spot with late staining	Halo of hyperfluorescence surrounding hypofluorescence spot	Nodular lesions of moderate reflectivity breaking through RPE
IV	Deep, punched-out, atrophic lesions	Early hyperfluorescence due to window defect	Dark spot	Regression of nodular lesions followed by incarceration of the outer plexiform layer and inner retina through RPE and Bruchs' membrane defects
V	Expanding atrophic lesion with increasing pigmentation	As above	Dark spot with surrounding late hyperfluorescence	Gradual loss of photoreceptor layer around the lesion and disappearance of the outer plexiform layer and inner retina

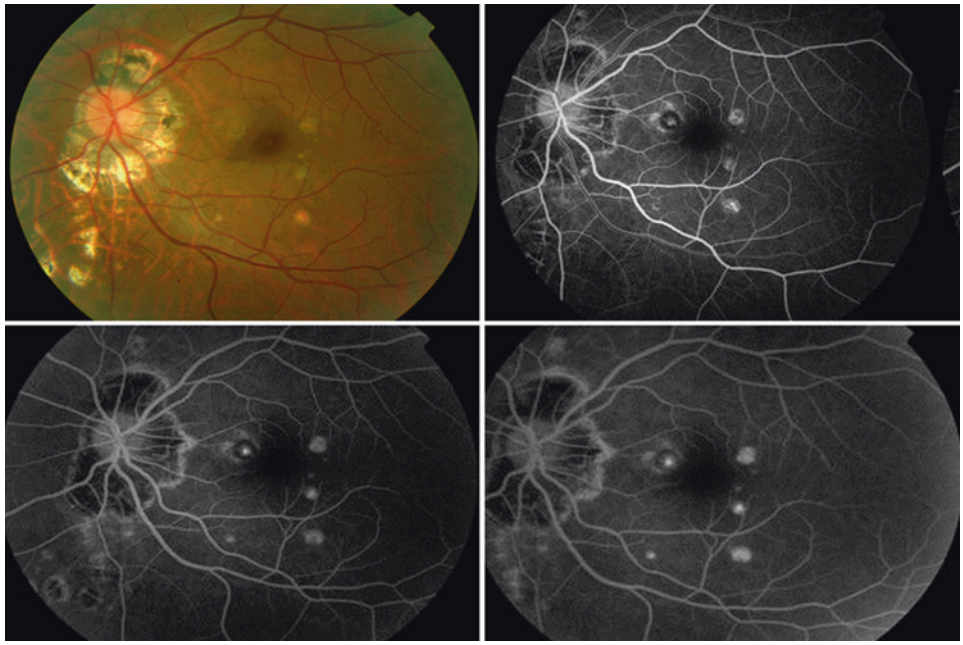


Punctate Inner Choroidopathy, Fig. 1 Autofluorescence in inactive disease shows typical patches of hypoautofluorescence

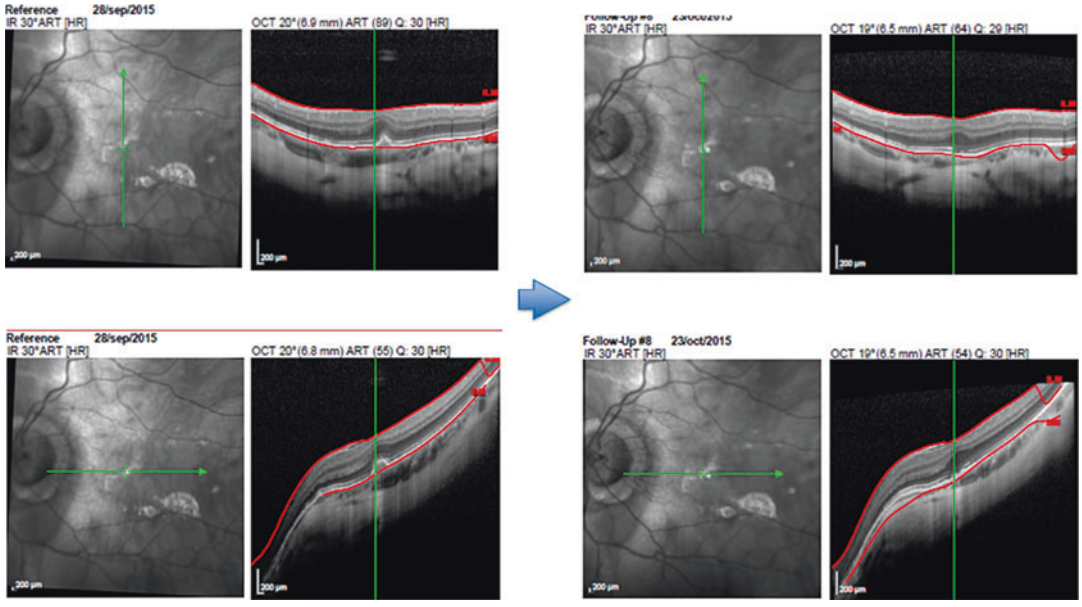
visible on clinical examination (Fig. 2), cystoid macular edema, and also to confirm CNVM formation. The features of PIC lesions on fundus fluorescein angiography (FFA) differ depending upon the stage of the disease: acute lesions are usually hyperfluorescent in the arterial and early arteriovenous phases, with late leakage, although a small proportion of eyes in the very acute stages of the disease may show early hypofluorescence and late staining; older or inactive lesions often demonstrate retinal pigment epithelium window defects, with central atrophic early hyperfluorescence. In cases where CNV develop, they appear as focal areas with a typical irregular lazy pattern, with early hyperfluorescence and late leak. Indocyanine green angiography (ICG) may be more sensitive than FFA: active lesions show early hypofluorescence that persists throughout the angiogram and becomes more apparent in the late phases and that may represent localized areas of choroidal hypoperfusion during the acute phases of inflammation. In addition to this, hyperfluorescence points seen along large choroidal vessels may be the result of a much larger widespread vasculitic process.

Treatment

Controversy still remains over what constitutes the optimal treatment for the majority of patients



Punctate Inner Choroidopathy, Fig. 2 Fluorescein angiography of atypical PIC. The small central lesions are typical, although the extensive peripapillary changes are not. The lesion superonasal to the fovea is clearly apparent on angiography but less obvious on the colour photograph



Punctate Inner Choroidopathy, Fig. 3 Typical PIC pre- (*left* hand images) and post- (*right* hand images) 60 mg/day prednisolone for 7 days

with PIC in the absence of secondary CNV (Fig. 3). As with other noninfectious uveitis, corticosteroids remain the mainstay of therapy. However, given the relapsing nature of the PIC lesions, patients often remain symptom-free for extended periods of time. Periocular or intravitreal corticosteroids may also be sufficient to control the initial inflammatory response and limit the extent of RPE disturbance and posterior subretinal fibrosis formation.

Steroid-sparing agents such as T cell inhibitors or antimetabolite agents have been used in patients with multiple recurrences as maintenance therapy, although data regarding their efficacy remains limited.

Similarly, there is no standard protocol for the management of secondary CNV. Since its introduction in the early 2000s, photodynamic laser therapy (PDT) has been used for CNV associated with PIC, given its "classic"-type morphology on FFA. Other treatment options have included steroid either oral, periocular, or intravitreal, used either in isolation or in combination with PDT. Surgical removal of CNV (characterized as type 2 by Gass) has also been employed, with varying degrees of success. Anti-VEGF agents have been used in PIC-associated CNV on the basis that these drugs are useful in treating CNV in exudative age-related macular degeneration (AMD) and there is now strong evidence in the literature for the use and efficacy of bevacizumab and ranibizumab such that these drugs now form the mainstay of treatment.

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Pupil Center

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Synonyms

Pupillary center

Definition

Center of pupillary aperture.

Basic Characteristics

The pupil of the eye is a critical limiting factor in the optics of the visual system. When the pupil changes its size, it controls not only the amount of light available to the visual system but also the optics of the eye.

The exact size and location of the pupil are important in corneal refractive surgery.

In keratorefractive procedures, the relationship between the size and location of the optical zone and the pupil is crucial for a successful visual outcome. If the corneal ablation becomes decentered with pupils of large diameter, the patient may complain about glare, halos, or starbursts under low illumination.

There have been several studies of the change in centration of the pupil with changing size,

with the center of the pupil moving slightly nasally and superiorly as the pupil constricted (Yang et al. 2002).

According to the recommendations of the Optical Society of America working group and the American National Standards Institute, wavefront errors (WFE) are quantified with respect to the pupil center (Applegate et al. 2010).

Cross-References

- ▶ Aberrometry
- ▶ Glare, General
- ▶ Pupil Diameter
- ▶ Refractive Surgery
- ▶ Scoptopic Pupil Diameter
- ▶ Wave Front Analysis

References

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Pupil Diameter

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Synonyms

Pupil width

Definition

Measurement across pupillary aperture.

Basic Characteristics

In healthy subjects, pupils are circular and equal in size (3–5 mm). A variety of influences may cause variation in pupil size ranging between 1.5 mm (miosis) and 8 mm (mydriasis). A difference in size of more than 1 mm between the pupils of both eyes is called anisocoria (Schünke et al. 2007).

Pupil diameter can be affected by neurologic conditions such as an afferent pupillary defect or Horner's Syndrome as well as by sleepiness, pharmaceutical side effects, psychiatric disorders, or autonomic neuropathy in diabetes mellitus or trauma (Wilhelm and Wilhelm 2003).

Pupil diameter is a determinant of outcome after refractive surgery. Visual symptoms such as halos, star bursts, and glare may emerge after keratorefractive procedures with a small optical zone or implantation of phakic intraocular lenses (IOLs) in patients with large scotopic pupils. The eye has numerous optical aberrations that increase as the pupil dilates (Yang et al. 2002).

Precise pupil diameter measurement can be performed accurately by binocular simultaneous measurements using pupillometers (Kohnen et al. 2004; Schnitzler et al. 2000).

Cross-References

- ▶ Adie's Pupil (Tonic Pupil), Pharmacologic Testing
- ▶ Afferent Pupillary Defects, Relative (Marcus Gunn Pupil)
- ▶ Anisocoria
- ▶ Argyll Robertson Pupil
- ▶ Colvard Pupillometer
- ▶ Infrared Pupillometers
- ▶ Pupil Center
- ▶ Scoptopic Pupil Diameter

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Pupil Diameter Under Low Light Conditions

► Scoptopic Pupil Diameter

Pupil Dilation

► Pupil Stretch

Pupil Dilator

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Definition

Device for pupil extension during ocular surgery.

Indication

The use of pupil dilators should be considered in cataract surgery with small nondilating pupils, iris prolapse, and intraoperative floppy iris syndrome.

Contraindication

None.

Use and Dosage

Different devices are currently available for intraoperative pupil dilation. Iris hooks are applied for four to five point iris retraction. Iris hooks are placed in sideports 1 mm posterior of the corneoscleral junction. Alternatively, ring expanders may be used for pupil expansion. Ring expanders reduce the risk of iris-sphincter damage due to a circumferential expansion of the pupil. Different devices are available and should be used according to the surgeon's preference.

Adverse Reactions

Excessive stretching of the pupil may result in iris sphincter damage. Improper positioning and removal of pupil dilators may result in tears of the anterior capsule or iridodialysis.

Cross-References

► Cataract Surgery
► Intraoperative Floppy-Iris Syndrome
► Tamsulosin

Further Reading

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Pupil Irregularity Caused by Trauma

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Definition

The pupil can be irregular or show anisocoria from trauma to the iris itself or damage to the parasympathetic pathway from the ciliary ganglion, the third cranial nerve or central oculomotor nuclei, or damage to the oculosympathetic pathway to the dilator muscle.

Basic Characteristics

Evaluating for Abnormalities

The first step in evaluating anisocoria is to determine if the anisocoria is worse in the light or in the dark. If the anisocoria is worse in the light, then this suggests a problem in either the parasympathetic innervation to the sphincter pupillae or the iris. Normal adult pupils should be of equal size and depending on age are variable sized in diameter but typically 2–4 mm when observed in the light. In up to 20% of the population, there is a 1 mm or less anisocoria that is the same in the light and in the dark and is not pathologic. In trauma patients, however, unequal pupils should be evaluated as pathologic until proven otherwise.

Tonic Pupils

Tonic pupils are characterized by a large pupil that reacts sluggishly or not at all to light and better tonically to accommodation. Tonic pupils can result from trauma to the intraorbital ciliary ganglion or short ciliary nerves which results in parasympathetic denervation of the sphincter pupillae. On slit lamp biomicroscopy, there may be constriction of some segments of the pupil (i.e., vermiform movement) with absent constriction in other segments (i.e., sector paresis). Topical testing with low dose pilocarpine 1/10% might demonstrate denervation supersensitivity in the tonic pupil.

Hutchinson Pupil

Hutchinson pupil is characterized by anisocoria and ipsilateral mydriasis typically associated with other oculomotor nerve deficits. Rarely, isolated pupillary involvement in trauma cases may precede other signs of damage to the oculomotor nerve since the parasympathetic nerves are located peripherally to the oculomotor nerve (CN III). Hutchinson pupil commonly results in trauma patients due to increased intracranial pressure and secondary herniation of the uncus of the temporal lobe. The pupillary changes are usually seen on the same side as the herniation occurred but can occur as a false localizing sign on the contralateral side (Kernohan notch phenomenon). A fixed and dilated Hutchinson pupil in trauma is often associated with a higher risk for mortality.

Iris Sphincter Injury

Trauma to the iris sphincter pupillae can result from blunt or penetrating trauma to the eye

which causes mydriasis, dilation of the pupil, and a poor or no response to light and accommodation. Traumatic sphincter tears might be seen at the pupil margin. Traumatic uveitis can also lead to posterior synechiae that can cause a poorly reactive or fixed and dilated or miotic pupil. Slit lamp biomicroscopy should be able to differentiate these etiologies.

Horner Syndrome

Horner syndrome (HS) is characterized by sympathetic dysfunction that is associated with the classic triad of ipsilateral ptosis (eyelid drooping), miosis (pupillary constriction), and facial anhidrosis. A lesion anywhere along the three neuron sympathetic pathway can result in HS, although anhidrosis will only be present if the injury occurs at the level of the first or second-order neurons. The pupil that is experiencing these symptoms will also be slow to dilate in response to dark. Trauma often results in injury to the second-order neuron (e.g., carotid artery dissection) and may not have any additional signs or symptoms aside from other injuries sustained with the head or neck trauma. Horner syndrome in children is most often congenital and often is seen with birth trauma. There may be concomitant brachial plexus injury in patients with birth trauma.

Bilateral Mydriasis

When the pupils of both eyes are dilated and are sluggish to react to light or do not react at all in a patient with known or suspected trauma, this can be a poor prognostic sign of diffuse and severe brain and brainstem injury or secondary anoxia.

Cross-References

- ▶ Anisocoria of the Small Pupil
- ▶ Anisocoria: Big Pupil

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Pupil Stretch

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Synonyms

Pupil dilation; Pupilloplasty

Definition

Pupil stretch is a surgical technique to mechanically stretch small pupils and thus allow phacoemulsification in poorly dilated eyes (maximum pupil size 4 mm). Several surgical techniques are described to mechanically stretch small pupils. Techniques include the use of flexible iris hooks, mechanical dilating devices such as Beehler pupil dilator (Moria), the Perfect Pupil expansion ring (Becton Dickinson Ophthalmic Surgical), and performance of multiple partial iris sphincterotomies. Additional substances as ophthalmic viscosurgical devices are used for pupil stretch.

History

In 1992 Masket listed traditional methods for pupil enlargement such as synechiolysis by sector iridectomy, inferior or radial sphincterotomies, multiple incomplete sphincterotomies, and post-paced suture of iris defects. However, these surgical approaches are all due to aesthetically deformed or functionally deficient pupils. So in the following years, new surgical techniques for atraumatic pupil dilation were developed such as preplaced inferior iris suture (Masket), small pupil enlargement with self-retaining retractors and repositors (Mackool), or pupilloplasty (Fine). In modern cataract surgery with undilated pupils, most surgeons perform phacoemulsification through a small pupil using minimal iris manipulation.

Clinical Features

Intraoperative miosis due to aging, pseudoexfoliation, diabetes, uveitis, or chronic miotic therapy has been described as a risk of conversion from phacoemulsification to extracapsular cataract extraction. To avoid complications during the operation caused by miosis, different methods of pupil stretch have been developed.

Tests

Intra- and postoperative thorough examination of the anterior segment with the slit lamp or operating microscope, as well as postoperative pharmacological dilation of the pupil, and measurement of uncorrected and best spectacle-corrected visual acuity are mandatory to maintain best possible postoperative results.

Differential Diagnosis

There are no data available in this topic.

Etiology

See section "History" above.

Treatment

As described above there exist multiple techniques for pupil stretch. One surgical technique uses Rappazzo scissors. The procedure includes eight tiny sphincterotomies measuring 0.5–0.75 mm that are cut at equal intervals around the pupillary border and results in a considerable increase in pupil size. Another method incorporates the combination of a superior radial full sphincterotomy with preplacement of a superior iris suture. This technique with preplacement of the permanent iris suture assures proper alignment of the iris papillars and results in a physiologic pupil. Mackool designed for pupil stretch two new instruments – self-retaining iris retractors and an iris repository – and his method allows the iris to be securely and reversibly retracted in several meridians simultaneously.

Cross-References

- Iridotomy
- Iris Hooks

References

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Pupil Width

▶ Pupil Diameter

Pupil, Characteristics

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Definition

The pupil is the aperture at the center of the iris which normally enlarges during low lighting conditions and contracts during bright lighting conditions to control the amount of light admitted to the eye.

Basic Characteristics

Aqueous flows through the pupil from the posterior chamber to the anterior chamber. Restriction of this normal flow at the pupil can result in pupillary block and related narrow angle with or without elevation in intraocular pressure.

The iris sphincter muscle constricts the pupil in response to light. This pathway involves the optic nerve and optic tract, the Edinger-Westphal (oculomotor) nuclei, the oculomotor nerve, and the ciliary ganglion. The sympathetic system controls the dilator muscle of the iris.

When a light is shined into one eye, there is direct constriction of the pupil in that eye as well as a consensual constriction in the contralateral eye (because of bilateral stimulation of the Edinger-Westphal nucleus). The intensity of this response is proportionate to the light-carrying ability of the directly stimulated optic nerve.

If a lesion of the optic nerve is present, there may be an afferent pupillary defect (APD). An APD is present when the direct light pupillary response in the involved eye is less intense than its consensual response.

Not only does pupil size vary with lighting conditions, it also varies with age, between individuals, and with emotional states and alertness. The normal pupil also becomes smaller with accommodation.

Assessing pupil size and response to light and near stimuli can be used to measure optic nerve function and localize lesions along the visual pathway. For example, abnormal pupillary responses can identify problems along the afferent light pathway, the parasympathetic or sympathetic pathways, or a lesion in the brain. Pupils are normally similar in size but can be about 0.5 mm different from each other in 20–40% of normal individuals. Asymmetry greater than this is considered anisocoria.

Further Reading

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Pupillary Block

▶ Acute Angle Closure

Pupillary Center

▶ Pupil Center

Pupillary Light Reflex

▶ Light, Pupillary Response

Pupillometers

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Definition

Device for pupil size measurement.

Purpose

Assessment of pupil size under defined illumination levels prior to refractive surgery.

Principle

For pupil size measurement, either comparison charts (pupil cards), rulers, or infrared pupillometers may be applied. Currently, different infrared pupillometers are commercially available. The devices differ in measurement period, pupil margin detection (observer or software based), and monocular or binocular measurement and illumination level.

Indication

In refractive surgery, the optical zone should ideally exceed the pupil diameter under any level of ambient illumination in order to minimize the risk of night vision problems. Pupillometers enable the definition of minimum optical zones in refractive surgery.

Advantage/Disadvantage

Modern infrared pupillometers provide highly accurate and reproducible measurements of pupil size under standardized conditions. However, results may be influenced by retinal dark adaption, accommodation, alertness, emotional status, and different medications. Further difficulties arise since pupils are often asymmetric and highly dynamic.

Cross-References

▶ Optical Aberrations
▶ wg-LASIK

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Pupilloplasty

▶ Pupil Stretch

Pure Alexia

▶ Alexia, Without Agraphia

Pure Word Blindness

▶ Alexia, Without Agraphia

Purtscher's Like Retinopathy

► Amniotic Fluid Embolism, Purtscher-Like Retinopathy

PXF

► Pseudoexfoliation Syndrome

Pyogenic Granuloma

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Synonyms

Eruptive hemangioma; Granulation tissue-type hemangioma; Lobar capillary hemangioma

Definition

A highly vascularized, pedunculated conjunctival mass with fibrous base; a pyogenic granuloma is comprised of granulation tissue with chronic inflammatory cells, fibroblasts, and capillaries. It is often found over chalazion, postsurgically over vicryl sutures or in areas of chronic irritation. It resolves with topical corticosteroid and is neither pyogenic nor granulomatous, but rather a proliferative fibrovascular response.

Cross-References

► Chalazion
► Vascular Tumors Disease of the Conjunctiva

Further Reading

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Pyramidal Fracture (Le Fort II)

► Le Fort Fractures

Q

Q Factor-Optimized Ablation Profile

► Aspheric Profile Photorefractive Keratectomy

Q-Factor Customized Ablation Profile

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Synonyms

Aspheric ablation profile; Wavefront-optimized ablation profile

Definition

An ablation profile that aims at minimizing postoperative spherical aberration, by maintaining preoperative corneal asphericity (q factor).

Basic Characteristics

Corneal laser refractive surgery with conventional ablation profiles changes corneal asphericity (q factor). Myopia treatment changes the shape from prolate ($q < 0$) to oblate ($q > 0$). The optical result is an induction of positive spherical aberration which was found to be proportional to the attempted spherical equivalent (Applegate and Howland 1997; Moreno-Barriuso et al. 2001; Oshika et al. 2002). The fact that spherical aberration significantly deteriorates retinal image quality prompted the development of aspheric ablation profiles with less induction of spherical aberration than conventional profiles (Mrochen et al. 2004). Q-factor customized ablation profiles aim at maintaining the preoperative corneal q factor (Koller et al. 2006). The profile is calculated individually ("customized") based on preoperative corneal shape, the attempted treatment, and the programmed optical zone. A "fudge factor" for anticipating the loss of laser fluence in the corneal periphery can be included in the treatment algorithm.

A preoperative corneal topography to determine the preoperative corneal asphericity (q factor) is mandatory. Together with other data like refraction and aberrometry, programmed optical zone, and corneal pachymetry, these data are integrated in a proprietary treatment algorithm. The treatment itself is identical to a treatment with a conventional profile. The predictability of the ablation can be assessed with postoperative corneal topography or aberrometry.

Cross-References

► Aspheric Ablation Profile

U. Schmidt-Erfurth, T. Kohnen (eds.), *Encyclopedia of Ophthalmology*,
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R

Racemose Hemangioma

► Vascular Tumors Disease of the Conjunctiva

Radial Keratotomy

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Synonyms

Anterior radial keratotomy

Definition

Corneal incision performed to flatten the cornea and reduce myopia.

Epidemiology

Radial keratotomy was the most commonly performed refractive procedure in the late 1970s and 1980s.

History

Sato first described this procedure in 1939.

Clinical Features

No clinical feature data available for this topic.

Tests

Preoperative evaluation includes slit lamp examination, pachymetry and topography of the cornea, as well as BCVA refraction.

Differential Diagnosis

Corneal relaxation procedures for correction of myopia:

- Astigmatic keratotomy
- Arcuate keratotomy
- Transverse keratotomy
- Trapezoidal keratotomy
- Hexagonal keratotomy
- Limbal relaxing incisions

U. Schmidt-Erfurth, T. Kohnen (eds.), *Encyclopedia of Ophthalmology*,
https://doi.org/10.1007/978-3-540-69000-9

Etiology

Due to unstable results, radial keratotomy has been replaced by the far more accurate excimer laser.

Treatment

There are two methods for radial keratotomy. In the "American-style incision," the incisions are performed from the optical zone toward the limbus. The Russian centripetal technique described incisions starting at the limbus and continuing toward the optical zone. The "genesis technique" was a combined technique from the two others.

Cross-References

- ▶ Arcuate Keratotomy
- ▶ Astigmatic Keratotomy
- ▶ Hexagonal Keratotomy
- ▶ Limbal Relaxing Incisions
- ▶ Transverse Keratotomy
- ▶ Trapezoidal Keratotomy

Further Reading

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Radiance

- ▶ Brightness (Radiance)

Raised Conjunctival Lesions

- ▶ Papillae: Overview

Ranibizumab

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Definition

Ranibizumab (Lucentis; Genentech, South San Francisco, California) is the fragment of a recombinant humanized antibody Fab which binds and neutralizes the human vascular endothelial growth factor A (VEGF-A). Ranibizumab binds to VEGF-A with high affinity, thus preventing the interaction of VEGF-A to both its receptors VEGFR-1 and VEGFR-2. Ranibizumab binds to all VEGF molecules with a one-to-one ratio. Ranibizumab has a molecular weight of 48 kDa, is produced in *Escherichia coli*, and presents no glycosylation sites. It contains only the Fab fragment of the entire parental antibody bevacizumab (149 kDa) that is an entire humanized recombinant antibody and therefore contains both the Fab and Fc fragments of the molecules.

In vitro and in vivo studies have demonstrated a 5- to 20-fold higher activity of ranibizumab in comparison to bevacizumab and a shorter half-life, estimated in approximately 9.8 days. Because of the smaller molecular weight in comparison to the entire antibody, ranibizumab has a higher diffusive capacity from the vitreous to the retina and the choroid tissues.

VEGF-A has been demonstrated to play a pivotal role in the regulation of angiogenesis both under physiologic and pathologic conditions (Ferrara et al. 2003). As far as the eye is concerned, VEGF-A is produced by various cell populations, such as retinal pigment epithelial cells, neurons, glial cells, ganglion cells,

endothelial cells, Muller cells, and smooth muscle cells. The primary target of VEGF-A is vascular endothelial cells, although all cell populations are at least in part affected by its action. VEGF-A synthesis is regulated by variations of ocular oxygen tension. Under condition of normal oxygen pressure, the hypoxia-inducible factor 1alpha, which is the cell's oxygen sensor, is hydroxylated and degraded via the ubiquitin-proteasome intracellular proteolytic pathway. Under the condition of low intracellular oxygen tension, however, the rate of hydroxylation is reduced, and stabilized hypoxia-inducible factor 1alpha is capable to interact with nuclear VEGF-A genes, thereby inducing VEGF-A synthesis. The major effects of VEGF-A are the increase in hydraulic conductivity via the induction of fenestration of cell bodies and the activation of metalloproteinases and phosphorylation of various intracellular and junctional proteins which eventually lead to a loss of intracellular tight junctions. The final effects of VEGF-A are an impairment of blood/retinal barrier. Ranibizumab binds to VEGF-A, which becomes unavailable for the interaction with its receptors VEGFR-1 and VEGFR-2 and prevents the onset of the abovementioned molecular mechanisms which eventually would lead to the development of retinal edema, endothelial cell proliferation, and neovascularization.

Indications

Intravitreous ranibizumab injections are a valid therapeutic strategy for several retinal diseases.

Ranibizumab is the first VEGF-A inhibitors approved by the FDA for the treatment of diabetic macular edema (DME), which represents a prominent cause of visual loss in patients with diabetes mellitus and the most frequent cause of legal blindness among adult individuals in developed countries. In DME visual loss is caused by diabetes-induced microvascular damages which cause the thickening and structural alteration of the basal membrane and the loss of the pericytes and vascular endothelial cells. These events lead to microaneurysm formation and the impairment of the blood/retinal barrier. The consequent vascular leakage results in the development of DME. VEGF concentration was found to be increased in ocular fluid of patients with DME, and it was hypothesized that ranibizumab via its binding and inactivation of VEGF-A may stop the evolution of these pathological events. The clinical effects of ranibizumab in DME were evaluated in randomized clinical trials. The DRCR Network showed that patients treated with 0.5-mg ranibizumab plus prompt laser or deferred laser therapy had significantly better visual acuity outcomes at 1 year than those treated with sham injection plus prompt laser. The results were confirmed at 2-year follow-up. The RESTORE trial randomized patients with DME to either 0.5-mg ranibizumab monthly for 3 months and then as needed plus sham laser (group A), 0.5-mg ranibizumab monthly for 3 months and then as needed plus laser therapy (group B), or sham injections plus laser therapy (group C). At 1 year, visual acuity improved of six ETDRS letters with ranibizumab alone (group A), 5.9 letters with ranibizumab combined with laser (group B), and only 0.8 letters with laser alone (group C) ($P < 0.0001$, A and B vs. C). Mean central retinal thickness also significantly decreased in both ranibizumab groups compared with laser alone. Lately the RISE and RIDE trials confirmed the positive effects of ranibizumab for the treatment of DME (Aiello et al. 1994).

Another approved indication for ranibizumab is the treatment of neovascular age-related macular degeneration (AMD), characterized by a new vessel formation which takes origin from the choroid (Rosenfeld et al. 2006). Choroidal neovascularization development has been correlated to the elevated intraocular VEGF-A concentrations. Choroidal neovascularization is characterized by structural and functional alterations which lead to intraretinal bleeding and exudations, with subsequent impairment in retinal oxygen perfusion and focal hypoxic areas. In turn, focal hypoxia determines further VEGF-A synthesis with a self-perpetuating pathologic cycle.

The effect of anti-VEGF therapy was demonstrated by the MARINA trial involving patients with minimally classic/occult choroidal neovascularization, who were treated with fixed monthly intravitreal injections, gaining more letters of vision with respect to the sham-injected controls (improvement of 7.2 letters vs. loss of 10.4 letters). Approximately 95% of patients treated with ranibizumab maintained or improved visual acuity compared to 62% of eyes in the control group. Similarly, the ANCHOR trial demonstrated the superiority of ranibizumab over standard therapy (verteporfin photodynamic therapy) in the treatment of classic choroidal neovascularization. In particular, at 1-year follow-up, 94.3% of patients given 0.3 mg of ranibizumab and 96.4% of those given 0.5 mg lost less than 15 letters, as compared with 64.3% of those in the verteporfin photodynamic therapy group ($P < 0.001$). Visual acuity improved by 15 letters or more in one third of both ranibizumab subgroups, as compared with marginal improvement (5.6%) of the verteporfin group ($P < 0.001$). Mean visual acuity increased by 8.5 and 11.3 letters in the 0.3- and 0.5-mg ranibizumab group, respectively, as compared with a decrease of 9.5 letters in the verteporfin group ($P < 0.001$). The HARBOR trial enrolled four groups. For 12 months, two groups received monthly ranibizumab at doses of either 0.5 mg or 2.0 mg, and two groups received the same doses, but each on an as-needed basis after three monthly loading doses of ranibizumab. All subgroups showed a clinically meaningful visual gain over the first year of the study, ranging from a gain of 10.1 letters in the 0.5-mg monthly group to 8.2 letters in the 0.5-mg PRN group. At 12 months, the mean change in visual acuity was similar in the four treatment subgroups, although it was slightly lower in the 0.5-mg as-needed subgroup. At 24 months, most patients had lost approximately one letter from month 12, but patients in the 0.5-mg as-needed group lost only 0.3 letters. These data suggest that there is an individualized response to treatment and a need to individualize it in this patient cohort.

The National Institutes of Health funded a head-to-head trial to compare bevacizumab and ranibizumab, the "Comparison of Age-Related Macular Degeneration Treatments Trials (CATT)" study. The drugs performed comparably in both the monthly (ranibizumab, 8.5 letters gained; bevacizumab, 8.0 letters gained) and as-needed (ranibizumab, 6.8 letters gained; bevacizumab, 5.9 letters gained) treatment arms. Results at 1 year were confirmed at 2-year follow-up. Similar results were also achieved by another head-to-head trial, the IVAN trial, which was performed in the United Kingdom.

Meaningful results were obtained also with the ranibizumab treatment of retinal vein occlusions.

Branch retinal vein occlusions (BRVOs) and central retinal vein occlusions (CRVOs) afflict 1.8% and 0.5%, respectively, of the population over 50 years. Intravascular obstruction occurs at the arteriovenous crossings in BRVO and the lamina cribrosa in CRVO. The pathophysiologic mechanisms leading to retinal vein thrombosis are multifactorial and include both local and systemic factors including hypertension, diabetes mellitus, hypercoagulability as well as local hemodynamic changes (stasis and turbulence), and endothelial injury. Impaired venous outflow determines retinal ischemia.

Vitreous levels of VEGF-A in eyes affected by retinal vein occlusion are very elevated, suggesting that VEGF-A plays an important role in the pathogenesis of its complications, in particular of macular edema and retinal or iris neovascularization. Recently, two separate trials have evaluated the effects of monthly injection ranibizumab (0.3–0.5 mg) versus sham injections in the treatment of macular edema in patients with branch retinal vein occlusion (BRAVO) study or central retinal vein occlusion (CRUISE) study. Both studies demonstrated the efficacy of anti-VEGF treatment.

In the BRAVO study, ranibizumab determined a gain of 16.6 (at the dose of 0.3 mg) to 18.3 letters (at the dose of 0.5 mg) compared with a gain of 7.3 letters in the sham group at 6 months. Approximately 60% of eyes treated with ranibizumab gained at least 15 letters compared to 29% in the sham group. In the CRUISE study, results were also impressive. Ranibizumab resulted in a gain of 13 (at the dose of 0.3 mg) to 15 (at the dose of

0.5 mg) letters compared to a not significant change in the sham group. Approximately 50% of eyes treated with ranibizumab gained at least 15 letters from baseline compared with only 17% in the sham group. At 6 months, intravitreal anti-VEGF significantly improved visual acuity in both BRVOs (20/125 baseline vs. 20/55) and CRVOs (20/270 baseline vs. 20/135). Improvements in visual acuity were associated to a significant reduction in foveal thickness. Following the initial 6-month BRAVO and CRUISE study period, all groups, including the control groups, received ranibizumab on an as-needed basis for macular edema with persistent clinical improvement.

An additional clinical indication for intravitreal injection of ranibizumab is choroidal neovascularization secondary to degenerative myopia. Several trials studies have shown that intravitreal injection of ranibizumab is effective for primary treatment myopic subfoveal and non-subfoveal choroidal neovascularizations, leading to a remarkable visual gain.

Finally, it has been demonstrated that VEGF-A is highly expressed in vascular endothelial cells and retinal pigmented epithelium of patients with polypoidal choroidal vasculopathy, a retinal disorder with multiple aneurismal and polypoidal lesions in the choroidal vasculature. Anti-VEGF-A administration reduces the subretinal exudation, leading to a visual acuity improvement. A combined therapy with intravitreal ranibizumab injection and photodynamic therapy seems to provide further synergistic effects in the treatment of polypoidal lesions.

Contraindication

Well-established contraindications to the intraocular use of ranibizumab are previous episodes of hypersensitivity against anti-VEGF agents or against one of the additive components of the injectable preparation. In addition, ranibizumab should not be used in patients with active intraocular or periocular infections, either diagnosed or suspected. Similarly, ranibizumab is contraindicated in patients with septic or aseptic endophthalmitis. The systemic administration of other anti-VEGF agents represents a contraindication to its intraocular use. At present it is unclear whether macular ischemia, which may be concomitant to macular edema in various clinical conditions, is a contraindication for prolonged anti-VEGF treatment, because a worsening of macular ischemia in the long term cannot be definitely excluded.

Clinical Use and Dosage

Ranibizumab is administered through intravitreal injection in two different dosages of 0.3 and 0.5 mg. In general, the recommended dose is 0.5 mg in an injected volume of 0.05 ml. The minimal interval between ranibizumab administrations is 1 month, with a treatment strategy based on the characteristics of the underlying disease. The treatment is continued with monthly injection until there is a stabilization of visual acuity. If there is no significant effect on visual acuity within the first 3 months of treatment, discontinuation of treatment is recommended. Therefore it is of great clinical importance to monthly monitor the visual acuity of patients during treatment, in order to resume the administration whenever visual acuity decline is registered. Over the follow-up, optical coherence tomography plays an important role to achieve an accurate monitoring of changes of intraretinal fluid and edema in response to treatment and to detect a relapse of the disease.

Side Effects and Adverse Reactions

After the intravitreal injection of 0.5 mg of ranibizumab, the systemic concentrations of the antibody are extremely lower than the intravitreal ones (90.000 lower according to the manufacturer) and well below the level required to inhibit 50% of the systemic activity of VEGF. All studies reported that the rates of systemic events which have been associated with the systemic use of anti-VEGF inhibitors such as thromboembolism, hemorrhage, gastrointestinal perforation, systemic

hypertension, and proteinuria, following intravitreal administration of ranibizumab, are very low. In a recent large Medicare analysis, treatment with ranibizumab was not associated with increased risk of mortality, myocardial infarction, stroke, or bleeding in comparison to pegaptanib or phototherapy. Similar data were also reported by a pooled analysis of various European registries based on ranibizumab use in everyday clinical practice and by a systematic review of reported side effects with all anti-VEGF agents. For ranibizumab the calculated cumulative incidences for heart disease are reported to be less than 0.10% per 100 injections. The incidence rates of stroke and transient ischemic attack (TIA) were below or equal to 0.07 per 100 injections for both ranibizumab and bevacizumab. It should be pointed out, however, that patients undergoing ranibizumab treatment, because of the advanced age and high prevalence of diabetes and hypertension, have an elevated absolute risk profile for cardiovascular and cerebrovascular events which is to a large extent independent of the intraocular treatment. Therefore more than the absolute risk of events, the relative risk should be taken into account.

As far as systemic hypersensitivity reactions are concerned, very few cases with oral angioedema and generalized urticaria have been reported, all resolved with steroid therapy.

The CATT study reported a significant prevalence of various minor side effects during therapy with ranibizumab and bevacizumab; however, the relationship between side effects and anti-VEGF doses is unclear, with higher prevalence of side effects in lower treatment groups.

Data from the European registry (Holz et al. 2011) and systematic reviews (Van Der Reis et al. 2011) showed that ranibizumab is associated with a low rate of ocular events that could be either caused by intravitreal injection per se or by the use of VEGF inhibitors.

Less than 1% of patients experienced retinal pigment epithelial tear or intraocular pressure-related events, and $<0.3\%$ of patients developed traumatic cataract, vitreous hemorrhage, deterioration of retinal blood flow, endophthalmitis, intraocular inflammation, or retinal detachment. Annual incidence of endophthalmitis from European registry was lower than in controlled clinical trial. Endophthalmitis was reported after ranibizumab injections with incidence rates below or equal to 0.04 per 100 injections; both infectious and non-infectious endophthalmitis were reported. For retinal detachment, a cumulative incidence rate of 0.01 per 100 injections has been reported. The occurrence of RPE tears has also been related to an anti-VEGF injection; the incidence rates for ranibizumab were equal to or below 0.14 per 100 injections. The overall incidences of mild anterior chamber reactions and anterior chamber inflammations (including any events described as anterior chamber inflammation, iritis, iridocyclitis, uveitis, or vitritis) were 1.06 per 100 injections of ranibizumab. Subretinal and vitreous hemorrhage occurred for ranibizumab at a rate of 0.03 per 100 injections. It should be pointed out that intraocular hemorrhages are a complication that may also be associated with the natural course of the underlying neovascular retinal diseases. An increased intraocular pressure (IOP) may be caused by the intraocular injection per se or by the pharmacologic properties of the intravitreal drugs used. The rise in IOP may be transient or sustained. The cumulative incidence rate of increased IOP reported for ranibizumab was below 0.50 per 100 injections.

Cross-References

► Antivascular Endothelial Growth Factor

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RAPD (Relative Afferent Pupillary Defect)

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Synonyms

Marcus Gunn pupil

Definition

A relative afferent pupillary defect (RAPD) is a clinical sign used to detect a lesion/defect in the pupil pathway on the afferent side. The direct response of the pupil to light can be compared to the contralateral consensual response by swinging the light stimulus between the two pupils. The detection of the RAPD requires two eyes but only one working pupil (see reverse RAPD below). When shining light into each eye, the affected eye (i.e., with the RAPD) demonstrates a diminished direct response to light, and when the light swings to the normal unaffected eye, the abnormal pupil dilates. The presence of an RAPD typically indicates a problem in the ipsilateral afferent pathway involving the retina or the optic nerve but also may occur in lesions of the optic tract or the pretectal neurons connecting the afferent pathway of the pupil to the efferent pathway in the midbrain (i.e., a tectal RAPD).

Etiology

Any lesion of the anterior visual pupil pathway (pregeniculate) can cause an RAPD.

Retinal lesions (e.g., retinal detachment, retinoblastoma, central retinal artery, or vein occlusion), optic nerve lesions (e.g., optic neuritis, anterior ischemic optic neuropathy, optic atrophy), and suprasellar lesions (e.g., pituitary adenoma, meningioma, craniopharyngioma) can all produce an RAPD.

Occurrence

The epidemiology of an RAPD depends on the underlying etiology of the lesion.

Classification

Signs and Symptoms

An ipsilateral RAPD might be associated with loss of visual acuity or visual field if the retina, optic nerve, chiasm, and tract are affected. A tectal RAPD might not be associated with visual loss if the visual afferent pathway is

unaffected, and only the pupillary afferent fiber is affected in midbrain.

Cross-References

- ▶ Optic Neuritis: Overview
- ▶ Swinging-Light Test, for RAPD Identification

Further Reading

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Ray Optics

- ▶ Geometrical Optics

Ray Tracing

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Synonyms

Laser ray tracing

Definition

Technique to measure optical aberrations of the human eye.

Purpose

To objectify wavefront aberrations.

Principle

In ray tracing, a sequentially delivered laser beam coming from a point object enters the eye through different pupil locations to form a spot on the retina. The local aberrations in the beam's entry position in the pupil cause a focal shift of the retinal image.

The retinal spot pattern is captured by a charge-couple device (CCD) camera, and the displacement of each spot from the location of the reference ray is computed. These displacement data are used to provide information about the local wavefront slopes for the whole pupil area (Moreno-Barriuso et al. 2001; Rozema et al. 2005; Yoon et al. 2006).

Indication

To measure optical aberrations of the human eye, correlation with visual symptoms, wavefront sensing for preoperative evaluation of refractive surgical procedures.

Advantage/Disadvantage

Ray tracing relies on a good retinal reflection, which can compromise measurement accuracy in patients with retinal pathologies; sequential measurement limits the application for real-time dynamic measurements.

Cross-References

- ▶ Aberrometry
- ▶ Higher-Order Aberrations, Refractive Surgery
- ▶ Shack-Hartmann Aberrometry
- ▶ Wave Front Analysis

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Rebound Headache

► Analgesic Rebound Headache

Reconstructive Corneal Graft

► Tectonic Penetrating Keratoplasty, for Herpetic Keratitis

Reconstructive Surgery of Eyelid

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Synonyms

Eyelid reconstruction; Eyelid repair

Definition

Surgical correction of partial or full thickness defects of the upper and/or lower eyelids.

Indication

Reconstruction of the eyelid is indicated in defects that may lead to secondary complications such as exposure keratopathy, epiphora, lagophthalmos, eyelid malpositions, and/or eyelid notching if left untreated. The most common indications for repair are defects resulting from cancer resection surgery, including Mohs surgery, and trauma. Involvement of the lacrimal outflow system necessitates surgical repair and reconstruction.

Contraindications

Surgery should be deferred until the patient is medically stable and a suitable candidate for surgery in cases of trauma. Also more serious injuries, such as a ruptured globe, take precedence and should be repaired prior to the eyelid injuries. In patients with monocular vision or in children at risk of amblyopia development, techniques that obstruct vision such as lid-sharing techniques should be avoided.

Techniques and Principles

The goals of eyelid reconstruction are to recreate a maximally functional eyelid, with a stable eyelid margin, while maximizing symmetry and aesthetic outcome. In reconstruction of eyelid defects, the surgeon must consider several factors: the size and orientation of the defect, the depth of the defect and the structures involved, the patient's age and laxity of their tissues, and any history of previous surgeries or a history of radiation to the region. General principles of eyelid reconstruction include: choosing the least disruptive technique to properly reconstruct the eyelid, minimizing vertical eyelid tension to avoid eyelid malpositions particularly ectropion, maintenance of proper canthal position and tension, attention to the diagnosis and treatment of any lacrimal outflow system injuries, and preference for local flaps for reconstruction as opposed to full thickness skin grafts.

Eyelid defects not involving the eyelid margin can sometimes be repaired by direct closure if vertical tension on the eyelid, which can result from closure in the horizontal plane, can be avoided. Direct closure of circular anterior lamellar defects not involving the eyelid margin should be closed with a vertical scar to avoid vertical tension and potential for ectropion. Advancement flaps, rotational flaps, and/or transposition flaps can be utilized if direct closure is not feasible. The flaps are mobilized as a composite of skin and muscle and incisions are hidden in relaxed skin tension lines when feasible. Large defects not amenable to closure with local advancement flaps may warrant full thickness skin grafting. Appropriate donor sites for full thickness skin grafts to the eyelids include: redundant skin from the upper eyelid, postauricular skin, supraclavicular skin, and preauricular skin.

Direct full thickness layered closure may be used for upper and lower eyelid defects involving usually less than 33% of the eyelid margin. Depending on the degree of tissue laxity, addition of a canthotomy and cantholysis can provide improved mobilization allowing for direct closure in wounds involving up to 50% of the eyelid margin. The wound is converted to a pentagonal wedge to allow closure without bunching of tissues. The defect is closed in layers. The keystone sutures are those which reapproximate the tarsus, which are passed in a lamellar fashion facilitated by the use of a spatulated needle. The eyelid margin is then realigned and the edges of the eyelid margin everted with sutures passed in a vertical mattress fashion. Everting the eyelid margin with this vertical mattress suture helps to avoid subsequent healing with notch formation. The skin/muscle is then directly closed with sutures.

Larger defects involving greater than on average 33–50% of the eyelid margin often require independent reconstruction of the anterior and posterior lamellar defects, one of these surfaces must provide vascularized tissue. Techniques that may be utilized for the repair of large upper eyelid defects include the Tenzel semicircular flap, Cutler-Beard flap, tarso-conjunctival transposition flaps, or free tarso-conjunctival grafts under anterior lamellar advancement flaps. Repair of large lower eyelid defects can be achieved with the use of the modified Hughes procedure, Tenzel semicircular flaps, free tarso-conjunctival grafts, or other tarso-conjunctival substitutes such as ear cartilage or hard palate graft under a vascularized skin/muscle flap.

Outcome

A reconstructed functioning eyelid able to provide protection to the globe is the desired outcome.

Complications

Eyelid malpositions such as ectropion or entropion with their inherent problems may result. Excess tension or inadequate alignment may result in lid notching or wound dehiscence. Limited eyelid mobility secondary to myogenic or neurogenic injury may occur including blepharoptosis or lagophthalmos. Cosmetic deformities may result after any extensive eyelid reconstruction.

Cross-References

- ▶ Buccal Mucous Membrane Graft
- ▶ Canthal Reconstruction
- ▶ Cantholysis
- ▶ Canthotomy
- ▶ Cheek Elevation, in Eyelid Repair
- ▶ Cutler-Beard Procedure
- ▶ Hard Palate Graft
- ▶ Hughes Procedure/Modified Hughes Procedure, in Eyelid Repair
- ▶ Mustarde Flap
- ▶ Simple Rotational Flap
- ▶ Tenzel Flaps
- ▶ Tarsoconjunctival Graft
- ▶ Transposition Flaps, for Lateral Canthal Defects
- ▶ Z-Plasties

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Recoverin

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Synonyms

Cancer-associated retinopathy (CAR) antigen

Definition

Recoverin is a neuronal calcium-binding protein in the photoreceptor cells of the eye involved in the recovery phase of visual excitation and adaptation to background light. It modulates the life of photoexcited rhodopsin by inhibiting rhodopsin kinase, the regulator of rhodopsin phosphorylation. Reducing this inhibition of the kinase regulates sensory adaptation in the retina and prolongs the light sensitivity of rhodopsin. Closing photoreceptor channels is light dependent and causes calcium to decrease and keeps calcium-bound recoverin from inhibiting rhodopsin kinase, causing faster inactivation of activated rhodopsin. When not bound to calcium, recoverin remains in the cytosol, but when bound migrates to the disk membrane using its amino terminal myristoyl group as an anchor.

Clinical Presentation

Patients with cancer-associated retinopathy (CAR), a rare retinal degenerative disease, have elevated antibodies against recoverin-like proteins. Its mechanism is not clearly elucidated, but suggests a series of autoimmune reactions against components of the retina, primarily CAR antigen. CAR serum antibodies have been used to construct the CAR antigen cDNA library, which shares 90% homology to a bovine recoverin amino acid sequence.

Cross-References

▶ Cancer-Associated Retinopathy (CAR)

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Recoverin-Associated Retinopathy (RAR)

▶ Cancer-Associated Retinopathy

Recurrent Corneal Erosion

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Synonyms

Dystrophia smolandiensis variant; Franceschetti hereditary recurrent erosion; Hereditary recurrent corneal erosion

Definition

A disease characterized by poor adhesion of the epithelial cell layer to the basement membrane resulting in localized sloughing of the epithelium causing. The erosions may be secondary to trauma or occur spontaneously (Krachmer et al. 2011).

Etiology

Inheritance is autosomal dominant. Erosions can be secondary to minor trauma or occur spontaneously. Sometimes dust, smoke, dryness, and lack of sleep precipitate erosions (Weiss et al. 2008).

Clinical Presentation

Patients can present with foreign body sensation, photophobia, and ocular pain and redness. Blebs and haze are seen on examination of the cornea. Symptoms develop in the first decade of life and become less frequent and intense over time (Weiss et al. 2008).

Diagnosis

Diagnosis is made with clinical presentation and family history. Slit lamp examination reveals blebs and haze on the cornea. No changes consistent with epithelial basement membrane disease are seen with light microscopy (Weiss et al. 2008).

Differential Diagnosis

Differential diagnosis includes epithelial basement membrane disease, map-dot-fingerprint dystrophy, anterior membrane dystrophy, Cogan microcystic dystrophy, corneal abrasion, dry eye syndrome, corneal foreign body, herpes simplex, and Fuchs' corneal dystrophy.

Prophylaxis

Prevention is to avoid precipitating factors such as trauma, dust, smoke, or dryness. When precipitating factors cannot be avoid, hypertonic saline drops and ointments or topical lubricants are used (Krachmer et al. 2011).

Therapy

Various therapies are used in preventing and treating corneal erosions. The objectives of the treatments are the same, which is to promote corneal healing. Common treatments are topical lubricants, topical cycloplegics, antibiotic ointments, autologous serum tears, bandage contact lenses, and pressure patching. When conservative measures do not work, then epithelial debridement, corneal micropuncture, or phototherapeutic keratectomy can be performed (Krachmer et al. 2011). In severe cases that lead

to significant corneal scarring, a keratoplasty may be necessary to restore vision.

Prognosis

In the first few decades of life, prevention of recurring attacks of pain and foreign body sensation can be difficult to treat. However, attacks decline over time and often cease by the age of 50 years old (Weiss et al. 2008).

Epidemiology

The prevalence of recurrent erosion is unknown. Onset is usually the first decade of life.

Cross-References

- ▶ Epithelial Dystrophies
- ▶ Epithelial Erosions
- ▶ Fuchs' Dystrophy Disease
- ▶ Herpes Simplex Virus
- ▶ Map-Dot-Fingerprint Dystrophy (Epithelial/Anterior Membrane Dystrophy)

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Red Eye

- ▶ Adenoviral Keratoconjunctivitis

Red Rock Syndrome

- ▶ Interlenticular Opacification

Red-Green Color Vision, Defects

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Synonyms

Achromatopsia

Definition

Dyschromatopsia is a congenital or acquired disorder of color vision. The human retina has three types of cones, each optimally responding to one of the primary colors: blue-sensitive cones (coded on chromosome 7), red-sensitive cones, and green-sensitive cones (both coded on the

X-chromosome). The different colors of the spectrum are perceived by different mixtures of these three colors. Normal individuals are called *trichromats* (three-color system). In contrast, *dichromats* have only two functioning cone types, and monochromats only have one. The term "protanopia" refers to a defect in red perception, whereas "deuteranopia" is a defect in green perception and "tritanopia" is a defect in blue perception (Barrett et al. 2012).

Etiology

Mutations in the genes coding for the cones can cause congenital color blindness. The most common mutations occur in the X-chromosome and thus affect males much more commonly than females (see "Epidemiology").

Color blindness can also be an acquired condition resulting from lesions in the afferent visual pathway in one or both eyes (e.g., from optic nerve damage (such as in multiple sclerosis or advanced glaucoma), chiasm, optic tract to brain lesions (e.g., radiations or in the occipital lobe, specifically in the V8 region (Barrett et al. 2012). Optic nerve lesions tend to affect red-green, while retinal lesions affect blue-yellow more often (Ropper and Samuels 2009). However, the other conditions usually affect all colors (not necessarily to the same extent) and sometimes show other symptoms depending on the size and location of the damage.

Some medications can cause acquired dyschromatopsia (e.g., ethambutol used against mycobacteria. Erectile dysfunction agents (e.g., Sildenafil), a phosphodiesterase inhibitor, can also cause a reversible, transient blue-green change in vision. The drug can affect the retinal phosphodiesterase as well as the penile form (Barrett et al. 2012).

Clinical Presentation

Hereditary (congenital) colorblindness is usually noticed in childhood, when children use inappropriate colors in their artwork and other activities, for example, using brown instead of red for flowers. In acquired forms, patients may complain that colors look "washed out."

Diagnostics

Ishihara color plates (pseudoisochromatic plates) can be used to diagnose color blindness in the clinic. They consist of numbers or shapes made up of colored spots on a background of similar colored spots. The colors are ones that would be difficult for an affected person to distinguish from the background.

Differential Diagnosis

- Congenital Colorblindness
- Medication-induced color deficiency
- Optic neuritis
- Occipital lobe stroke (V8 region)

Prophylaxis

There is no known prophylaxis.

Therapy

Congenital red-green colorblindness cannot be cured. In acquired forms, the underlying problem should be treated.

Prognosis

Congenital color blindness-affected individuals may have variable limitations in certain occupations but in general can use environmental cues to guide them in leading a normal life. For example: a vertical traffic light has red as the top color and green as the bottom color. If the color blindness is acquired, then the prognosis depends on the severity and type of disease or lesion.

Epidemiology

Since this is commonly an X-linked-inherited and recessive disorder, males are affected if they get the affected X-chromosome and females become carriers and may pass the gene onto half of their sons. If however the gene on both X-chromosomes is mutated, a female can be affected. About 8% of the Caucasian male US population and 0.4% of the female population are affected (Barrett et al. 2010) by congenital color blindness. The epidemiology of acquired dyschromatopsia is dependent upon the specific etiology.

Cross-References

- ▶ Color Vision Deficiency
- ▶ Optic Neuritis: Overview

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Red-Green/Duochrome

- ▶ Bichrome (Red-Green/Duochrome) Test

Reflection Law

- ▶ Law of Reflection: Definition

Reflex Blepharospasm

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Synonyms

Secondary blepharospasm

Definition

Blepharospasm is spasm of the eyelids. Bilateral benign essential blepharospasm (BEB) can be an adult-onset localized dystonia involving spontaneous contractions of the periocular muscles, namely, the orbicularis oculi, procerus, and corrugator muscles. This results in bilateral eye closure that ranges in severity from a benign increase in blink frequency to severe impairment from sustained eyelid closure. Blepharospasm typically has a gradual and intermittert onset occurring during midlife after age 30. Reflex blepharospasm is a type of secondary blepharospasm triggered by dry eyes, blepharitis,

intraocular inflammation, meningeal irritation, and light sensitivity.

Etiology

In contrast to reflex blepharospasm, BEB has no known etiology.

Clinical Presentation

Clinical manifestations of blepharospasm include an increase in blink frequency and spastic involuntary closure of the eye. Though it can present asymmetrically, blepharospasm is typically bilateral, synchronous, and symmetric. The criteria suggested for diagnosing blepharospasm are synchronous orbicularis oculi spasms resulting in bilateral eyelid narrowing/closure as well as either an increase in blink frequency and/or a "sensory trick" maneuver that decreases the dystonia. Patients with reflex blepharospasm usually have worsening of symptoms with bright light or stress, with onset typically beginning with dry eye or ocular irritation due to photosensitivity. Reflex blepharospasm may be triggered by photosensitivity and surface disease.

Diagnostics

Blepharospasm is a clinical diagnosis made by a thorough history and physical examination.

Differential Diagnosis

Blepharospasm should be distinguished from Meige syndrome or craniocervical dystonia, which includes both the focal dystonic eyelid closure of blepharospasm in addition to contractions of the lower face, jaw, and neck. Meige syndrome involves bilateral contractions of the face. Though most cases of Meige syndrome are due to an unknown etiology, it can result from prolonged neuroleptic medication use. Blepharospasm should also be distinguished from hemifacial spasm (HFS) which is involuntary unilateral facial spasms that often start with the eyelid. HFS is typically transitory and clonic movements and, unlike blepharospasms, is usually unilateral, with less than 5% being bilateral. Irregular, brief clonic movements begin in the orbicularis oculi and then spread to other muscles innervated by the facial nerve, gradually over months to years. Both BEB and HFS are most effectively treated by botulinum injections. EEG may be required in atypical cases where seizure is suspected but usually BEB and HFS are clinical diagnoses.

Therapy

In secondary causes instigating the reflex blepharospasm, the underlying etiology should be treated. Botulinum toxin is a potent neurotoxin made by *Clostridium botulinum* resulting in regional muscle weakness. Botulinum toxin may be further enabled through its zinc endopeptidase disrupting fusion proteins, thus interfering with acetylcholine release at the neuromuscular junction and causing localized muscle weakness. Botulinum toxin treatment is effective for up to 50–85% of patients with blepharospasm.

Prognosis

If the underlying secondary etiology is treated, symptoms may resolve.

Epidemiology

Age seems to be the most significant risk factor in blepharospasm development compared to other causes of focal dystonia. The mean age at onset of blepharospasm together with cranial dystonia was 55.7 years. One case control study in Italy showed that coffee drinking was associated with decreased development of blepharospasm compared to controls with the strength of the relationship increasing with average numbers of coffee cups per day. Patients with blepharospasm are also more likely to experience spread of the dystonia to other body parts (31% past the head) than other types of dystonias, with the greatest risk being present in the first 5 years of the disorder.

Cross-References

▶ Blepharospasm

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Reflex Tear Arc

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Synonyms

Lacrimation reflex

Definition

The reflex tear arc is responsible for production of tears in response to irritation of the ocular surface and in maintaining a tear film for adequate lubrication of the eye.

Structure

The reflex tear arc is triggered by ocular surface irritation and consists of the lacrimal glands, ophthalmic branch of the trigeminal nerve, and parasympathetic fibers from the superior salivary nucleus. The lacrimal gland is located in the superior lateral corner of the orbit, within the lacrimal fossa of the frontal bone. Inferiorly, it is in contact with the globe, and superiorly it is split into the upper (orbital) and lower (palpebral) lobes by the lateral horn of the levator aponeurosis. Approximately 8–12 lacrimal gland ducts empty into the superior cul-de-sac approximately 5 mm above the lateral tarsal border. The ducts from the orbital lobe join with the ducts from the palpebral lobe.

The ophthalmic branch of the trigeminal nerve serves as the afferent (sensory) pathway for detecting ocular surface irritation. The efferent pathway is composed of parasympathetic fibers originating from the superior salivary nucleus of the pons and traveling with the facial nerve. The lacrimal fibers leave the greater superficial petrosal nerve (branch of the facial nerve) and pass to the sphenopalatine ganglion. The fibers then enter the lacrimal gland via the superior branch of the zygomatic nerve through an anastomosis between the zygomaticotemporal nerve and the lacrimal nerve.

Along with the primary lacrimal gland, the accessory lacrimal glands of Krause and Wolfring are also responsible for aqueous tear secretion. These glands are smaller than the primary lacrimal gland; the glands of Krause are located in the upper fornix, while the glands of Wolfring are situated further down on the eyelid, above the tarsus.

Function

The reflex tear arc primarily produces tears from the main lacrimal gland in response to ocular

surface irritation. The accessory lacrimal glands of Krause and Wolfring provide nonreflexive, basal tear secretion. Aqueous secretion from the main and accessory lacrimal glands is composed of water, electrolytes, and proteins. This aqueous secretion combines with mucin from goblet cells to produce an evenly distributed tear film, which is coated by oily outer layer produced by the Meibomian glands that reduces evaporation of the tear film.

Clinical Relevance

Lacrimal gland tumors, although rare, require a thorough workup to differentiate benign from malignant lesions. Approximately half of lacrimal gland tumors are malignant, which often warrants obtaining a lacrimal gland biopsy of suspicious masses. Since the ducts from the orbital lobe join with the ducts from the palpebral lobe prior to emptying, lacrimal biopsy of the orbital lobe should be performed as biopsy of the palpebral lobe may seriously reduce secretion from the entire gland.

Keratoconjunctivitis sicca, i.e., dry eyes, is a common condition that can occur with reflex tear arc malfunction (Dartt 2004). Autoimmune diseases, e.g., Sjogren's disease, can affect the nerve innervation of the lacrimal glands, leading to inefficient tear production and ocular surface irritation. The ocular surface and the afferent limb of the reflex tear arc may be injured during corneal procedures, e.g., refractive surgery, leading to an abnormal reflex tear arc.

Crocodile tears syndrome, a.k.a., gustolacrimal reflex, is a unilateral lacrimation that occurs when a patient eats or drinks (Montoya et al. 2002). Crocodile tears syndrome usually follows a Bell's palsy or traumatic facial paralysis or can occur congenitally after a Duane's retraction syndrome. The underlying mechanism of this abnormal reflex is largely due to the misdirection of regenerating gustatory fibers from either the facial or glossopharyngeal nerves. While debilitating for patients, injection of botulinum toxin type A into the affected lacrimal glands may provide symptomatic relief.

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Refraction

▶ Refractive Ametropia

Refraction Law

▶ Law of Refraction (Snell's Law)

Refractive Ametropia

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Synonyms

Refraction; Refractive errors

Definition

In the ideal eye, an object located at infinity is sharply imaged to the retinal plane in the absence of accommodation. If the optics of the eye do not focus properly to the retina, it shows refractive ametropia. The most common forms of ametropia are myopia (nearsightedness)/hyperopia

(farsightedness), where the image plane is located in front of/behind the retinal plane or astigmatism. Ametropia refers to all refractive vision disorders or errors.

Cross-References

- ▶ Accommodation, Cataract
- ▶ Emmetropia: Definition
- ▶ Refraction
- ▶ Refractive Errors

Refractive Astigmatism

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Synonyms

Nonstigmatic refraction

Definition

Astigmatism is an optical disorder in which vision is blurred due to the inability of the optics of the eye to focus a point object into a conjugated image on the retina due to an irregular (mostly toric) curvature of the cornea or lens. The two types of astigmatism are regular (which can be compensated with optical corrections, e.g., glasses) and irregular (which cannot be compensated). Refractive astigmatism is caused by a difference in degree of curvature refraction of the two different meridians.

Cross-References

- ▶ Ametropia: Definition
- ▶ Refractive Errors

Refractive Errors

- ▶ Refractive Ametropia

Refractive Eye Surgery

- ▶ Refractive Surgery

Refractive Lens Exchange

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Synonyms

Clear lens exchange (CLE); Clear lens extraction; Refractive lens extraction (RLE)

Definition

Refractive lens exchange (RLE) is an essential ▶ cataract surgery without any cataract. The ▶ crystalline lens is removed and replaced with an artificial ▶ intraocular lens (IOL). The IOL is of a power to correct the underlying ▶ refractive error.

Epidemiology

RLE accounts for a marked amount of refractive surgeries in the presbyopic age group.

History

Early in the year 1890, Fukala reported on refractive lens extraction in eyes with high myopia

(Fukala 1890). This procedure was subsequently abandoned due to the tenfold increase of postoperative retinal detachment in comparison to unoperated myopic eyes. Since 1890, ophthalmic surgery has undergone steady changes by means of innovations in intraocular lens design, application of ophthalmic viscoelastic substances, and development of phacoemulsification and microincisional surgical techniques. These innovations improved the safety and efficacy of refractive lens exchange, making it an integral part of refractive surgery today.

Clinical Features

Implanted IOL are the same as used for cataract surgery. In the scope of RLE, toric and multifocal/accommodative IOL are especially in the focus of interest.

Tests

Indications for RLE are high myopia or hyperopia with coexistent presbyopia. The reason for the inclusion of presbyopia is the fact that RLE always leads to a complete loss of accommodation. Correction of underlying regular astigmatism in scope of RLE, which cannot be managed by corneal incisional techniques, is best accomplished by implantation of toric lens implants. Border indications for RLE are presbyopia without ametropia implying implantation of a multifocal lens implant, presbyopia with underlying astigmatism, and prepresbyopic patients with high hyperopia of +5 to +10 D not amenable for keratorefractive surgery or phakic IOL due to shallow anterior chamber situation (Kohnen 2011).

Differential Diagnosis

If any clinically relevant clouding of the crystalline lens is present prior to surgery, one should better declare surgery as cataract surgery.

Etiology

Compared to excimer and femtosecond laser surgery for refractive surgery, RLE is by far an older surgical procedure.

Treatment

Surgery and complication spectrum of RLE are similar to that following cataract surgery with some differences. Phacoemulsification is much more easy to perform and requires less phacoenergy as the lens does not incorporate a hard nucleus. Regarding the anatomy of the treated eyes, RLE is implemented in very short or very long eyes. From this specific situation, certain risks emanate the postoperative retinal pathologies after myopic RLE and typical intraoperative difficulties induced by short anterior segment in hyperopic RLE. Myopic RLE may be difficult due to instability of the capsular bag. This bears an increased risk for tear of the capsule. Insertion of a capsular tension ring might alleviate the intraoperative situation, especially in cases of weak zonules or lysis of the zonules. In eyes with high axial length, the risk of an intraoperative subchoroidal hemorrhage is markedly increased as compared to that in normal eyes. In eyes with an axial length of more than 25 mm, rare capsular block syndrome appears more frequently. Hyperopic RLE surgery in eyes with an axial length below 21 mm is hampered by the narrow spatial situation and shallow anterior chamber. Compared to eyes with normal axial length, the risk of choroidal effusion syndrome is markedly increased.

Cross-References

- ▶ Accommodative Intraocular Lens
- ▶ Cataract Surgery
- ▶ Intraocular Lens
- ▶ Multifocal Intraocular Lens
- ▶ Phacoemulsification and Posterior Chamber Intraocular Lens (IOL) Implantation

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Refractive Lens Extraction (RLE)

▶ Refractive Lens Exchange

Refractive Surgery

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Synonyms

Refractive eye surgery

Definition

Eye surgery used to correct refractive and eliminate or reduce a patients' need for wearing eyeglasses or contact lenses.

Basic Characteristics

One must differentiate between laser (flap and surface procedures) and non-laser refractive surgery.

Laser eye surgery can be divided into flap and surface procedures. Flap procedures include automated lamellar keratoplasty (ALK) and laser-assisted in situ keratomileusis (LASIK).

Surface procedures are Epi-LASIK, laser-assisted subepithelial keratomileusis (LASEK), and photorefractive keratectomy (PRK).

Non-laser refractive surgery includes implantable lenses, intrastromal corneal ring segments (Intacs), conductive keratoplasty (CK), astigmatic keratotomy (AK), radial keratotomy (RK), and limbal relaxing incisions (LRI). RK, AK, and LRI are counted among corneal incision procedures.

Cross-References

▶ Anterior Lamellar Keratoplasty (ALK)
▶ Astigmatic Keratotomy
▶ Conductive Keratoplasty
▶ Free Caps, LASIK Complication
▶ Limbal Relaxing Incisions
▶ PRK
▶ Radial Keratotomy
▶ Wavefront-Guided LASIK

Further Reading

Albert DM, Miller JW, Azar DT (2008) Albert & Jakobiec's principles & practice of ophthalmology. Saunders, Philadelphia

Regional Anesthesia

▶ Anesthesia (Anesthetics), Local
▶ Local Anesthesia for Ophthalmic Procedures

Reis-Bücklers Dystrophy

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Synonyms

Anterior limiting membrane dystrophy, type I (ALMD I); Atypical granular corneal dystrophy; Corneal dystrophy of Bowman's layer, type

I (CDB I); Geographic corneal dystrophy; Granular corneal dystrophy, type III; Superficial granular corneal dystrophy

Definition

A corneal dystrophy of Bowman's layer characterized by geographic opacities and recurrent erosions that lead to ocular pain and early visual loss (Figs. 1, 2, and 3).

Etiology

Inheritance is autosomal dominant.

Clinical Presentation

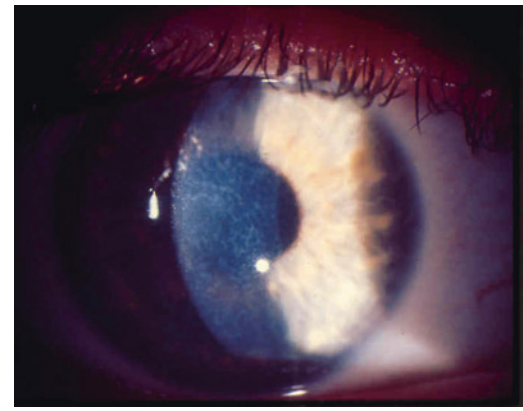
Patients have decreased vision at a young age (first or second decade of life) accompanied with pain and erythema from recurrent erosions. Confluent central geographic-like opacities involving Bowman's layer and the anterior stroma are seen on slit lamp examination (Krachmer et al. 2011).

Diagnostics

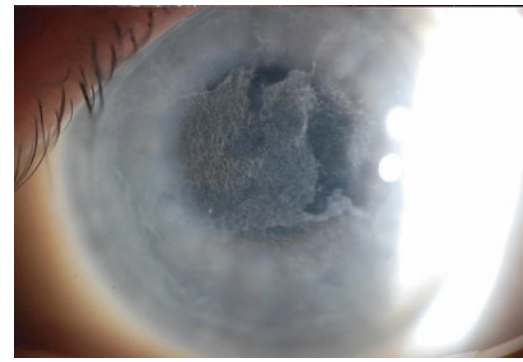
Transmission electron microscopy helps distinguish Reis-Bücklers dystrophy from Thiel-Behnke by identifying rodlike granules instead of curly fibers (Krachmer et al. 2011). In light microscopy Masson trichrome stain reveals sheet-like connective tissue substance replacing Bowman's layer. Confocal microscopy demonstrates highly reflective deposits in and replacing Bowman's layer (Weiss et al. 2008).

Differential Diagnosis

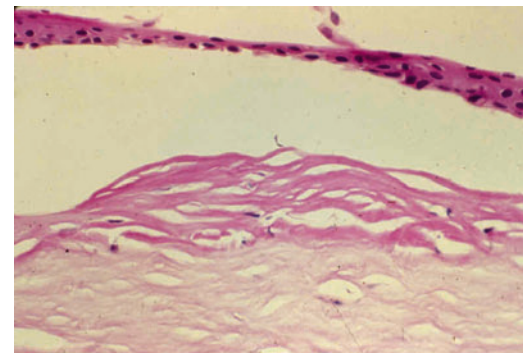
Differential diagnosis includes Thiel-Behnke corneal dystrophy, map-dot-fingerprint dystrophy disease, recurrent corneal erosion disease,



Reis-Bücklers Dystrophy, Fig. 1 Geographic opacities most prominent centrally



Reis-Bücklers Dystrophy, Fig. 2 Magnification of geographic opacities



Reis-Bücklers Dystrophy, Fig. 3 Histology – connective tissue-like substance replacing Bowman's layer

macular corneal dystrophy, Fuchs' corneal dystrophy, and herpes simplex.

Prophylaxis

No prophylaxis is known; however, topical lubricants are used to prevent corneal erosions.

Therapy

Treatment is initially focused on recurrent erosions that begin in the first or second decade of life. Topical lubrications, contact lenses, and patching are used during this time. Eventually, as corneal scarring develops, superficial keratectomy or phototherapeutic keratectomy (PTK) may be performed. Keratoplasty, lamellar or penetrating, is reserved for when the scarring becomes severe and deep. The dystrophy frequently recurs in the graft (Krachmer et al. 2011).

Prognosis

Recurrent erosions lessen with time. Vision slowly and progressively deteriorates until surgical treatment is necessary (Weiss et al. 2008).

Epidemiology

The condition is rare and prevalence unknown.

Cross-References

- ▶ Fuchs' Dystrophy Disease
- ▶ Herpes Simplex Virus
- ▶ Macular Corneal Dystrophy (MCD)
- ▶ Map-Dot-Fingerprint Dystrophy (Epithelial/Anterior Membrane Dystrophy)
- ▶ Recurrent Corneal Erosion
- ▶ Thiel-Behnke Dystrophy

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Relative Afferent Pupillary Defect (RAPD)

▶ Marcus Gunn Pupil

Residual Stroma Bed

▶ Residual Stroma Thickness

Residual Stroma Thickness

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Synonyms

Residual stroma bed

Definition

The amount of corneal tissue which is left, i.e., after LASIK. According to the Food and Drug Administration, a minimum of 250 μm of residual stroma thickness should be left under the LASIK flap in order to avoid corneal ectasia.

Epidemiology

No epidemiological data available.

History

Since LASIK has been performed in the late 1980s, the residual stroma thickness also became a term in refractive surgery.

Clinical Features

No clinical feature data available for this topic.

Tests

The residual stroma thickness can be measured by ultrawave pachymetry, anterior segment optical coherence tomography, or corneal topography.

Differential Diagnosis

Corneal treatment procedures which are dependent on the stroma thickness are as follows:

- LASIK
- LASEK
- PRK

Etiology

See History section above.

Treatment

See cross-references for an exact description of the different treatment methods involving the stroma thickness.

Cross-References

▶ Cornea
▶ wg-LASIK

Further Reading

Albert DM, Miller JW, Azar DT (2008) Albert & Jakobiec's principles & practice of ophthalmology. Saunders, Philadelphia

Residual Stromal Bed

▶ Stromal Bed

Respicort

▶ Intravitreal Triamcinolone

Retaane

▶ Anecortave Acetate (RETAANE), for Age-Related Macular Degeneration

Reticulum Cell Sarcoma (Old)

▶ Intraocular Lymphoma

Retina, Structure of

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Definition

A highly organized and specialized structure consisting of alternate layers of cell bodies and synaptic junctions that captures and transduces light images into a pattern of neuronal activity ultimately conveying visual information to the brain (Chen et al. 2006; Loewenstein and Green

1999; Miller 2006). It is located on the interior posterior surface of the eye.

Basic Characteristics

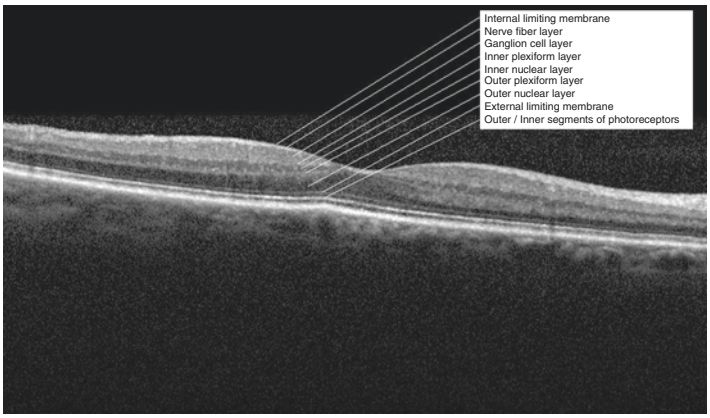
Histologically, the retina is composed of nine layers. These include (progressing from the outer retina to inner retina):

1. Layer of the outer and inner segment of the photoreceptors
2. External limiting membrane
3. Outer nuclear layer
4. Outer plexiform layer
5. Inner nuclear layer
6. Inner plexiform layer
7. Ganglion cell layer
8. Nerve fiber layer
9. Internal limiting membrane

All layers function together for the purpose of converting light images into neuronal signals, which can be interpreted by the brain as vision.

Layers 1 through 4 are in the deepest levels of the retina and involve the photoreceptor rod and cone cells of the retina. In the human eye, there are approximately 100 million retinal rod cells and five million retinal cones cells. The outer segments of these photoreceptor cells (layer 1) contain visual pigment stacked on disk membranes. When as little as one photon of light is absorbed by these light-sensitive pigments, the photoreceptor undergoes hyperpolarization and begins the process of transducing light energy into a neuronal signal. Retinal rod cells are far more sensitive to absorbing light than cones, likely due to their large content of the visual pigment rhodopsin, but are insensitive to color and have low special acuity. Outer segments of both rod and cone cells receive support from surrounding villous processes of the retinal pigment epithelium. They also receive support from their respective inner segments, which contain the protein synthesis and metabolic machinery for that photoreceptor cell. Both the outer segment and the inner segment lie distal to the external limiting membrane (layer 2). The outer nuclear layer (layer 3) is composed of nuclei of both retinal cone and rod cells. The outer plexiform layer (layer 4) involves the proximal ends of the photoreceptor cells. It is here that the photoreceptors connect with horizontal cells, bipolar cells, and second-order neurons via glutamate neurosynaptic junctions, to complete the transduction of light energy to a neurological signal. Horizontal cells are interneurons of the outer retina. They receive input from certain photoreceptor terminals, travel laterally, and reconnect to other photoreceptors terminals.

The inner nuclear layer (layer 5) contains nuclei of bipolar cells, amacrine cells, and interplexiform cells. Bipolar cells conduct signals from photoreceptors to ganglion cells in the inner plexiform layer (layer 6). Amacrine cells are the horizontal cells of the inner nuclear level and



Retina, Structure of, Fig. 1 Optical coherence tomography demonstrating nine layers of the retina

conduct signals between ganglion cells and other amacrine cells. Two types of bipolar cells exist, namely, depolarizing and hyperpolarizing. These cells for the basis for the on and off ganglion cell receptive field. Amacrine cells employ a variety of neurotransmitters, including peptides, gamma-aminobutyric acid (GABA), glycine, acetylcholine, and dopamine. Interplexiform cells are a relatively newly discovered type of cell and likely function to carry information from the inner retinal to the outer retinal, which is opposite to the direction of most signals in the retina.

The ganglion cell layer (layer 7) involves ganglion cells whose axon extends from the retina to the brain. These cells constitute the final common pathway for transduction of light from the photoreceptors of the retina to the brain.

The nerve fiber layer (layer 8) contains axons from ganglion cells on their way to the brain. These axons are unmyelinated in the human retina since myelination ceases at the lamina cribrosa during embryologic development. Rarely, some axons may appear myelinated in the retina.

The most internal layer of the retina is the internal limiting membrane (layer 9). This layer is composed of the basal lamina of Muller cells. It is thickest in the posterior fundus and becomes thinner as one moves more anterior. It is absent both over the foveola and the optic nerve (Fig. 1).

Cross-References

- ▶ Bipolar Cells
- ▶ Photoreceptor Cells
- ▶ Retinal Pigment Epithelium

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Retinae (Retinal Angiomatosis, von Hippel Syndrome/Disease)

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Synonyms

Angiomatosis retinae; Cerebelloretinal hemangioblastomatosis; Familial cerebello-retinal angiomatosis; Hippel Disease; Hippel–Lindau syndrome, HLS; Lindau disease or retinocerebellar angiomatosis; Von Hippel–Lindau disease, VHL

Definition

See the main entry "▶ Familial Cerebello-Retinal Angiomatosis)."

Cross-References

- ▶ Familial Cerebello-Retinal Angiomatosis

Retinal Arteries and Retinal Veins

► Retinal Blood Vessels

Retinal Blood Vessels

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Synonyms

Retinal arteries and retinal veins

Definition

The retinal blood vessels originate from the central retinal artery and permeate the retina from the internal limiting membrane to the inner nuclear layer to nourish and remove waste from the inner two thirds of the retina. This blood supply is completely independent of the choroidal vasculature.

Structure

The central retinal artery, a branch off of the ophthalmic artery, enters the eye by way of the optic nerve and branches into four retinal arteries that each supplies a different quadrant of the retina. Retinal arteries and veins remain in the nerve fiber layer of the retina. Smaller arterioles and venules extend deeper into the retina and create two microvascular networks: (1) a more superficial capillary bed in the ganglion cell and nerve fiber layer and (2) a deeper network in the inner nuclear layer. These capillary networks thin to one layer near the fovea and in the periphery. In the peripapillary region of the retina, a distinct layer of radial capillaries can be found in the inner nerve fiber layer, making these the most anterior of all capillary networks.

Capillary-free zones exist around larger retinal arteries, likely due to increased oxygenation of the retina in these locations. Retinal capillaries are also absent in the 400–500 μm foveal avascular zone and in the far periphery.

After the first retinal branch, the retinal arteries do not contain any elastic fibers or internal elastic membrane. Retinal capillaries consist of endothelial cell that are surrounded by pericytes. Retinal vein and venules generally follow their associated retinal arteries and arterioles. Where retinal arteries and veins cross, the artery usually is more anterior, and the arteries and veins share a common adventitial sheath.

After the ophthalmic artery enters the lamina cribrosa, there is no evidence of nerve fiber endings in retinal blood vessels. Therefore no central regulation of blood flow occurs within the retina but instead blood flow regulation is a result of autoregulation due to changes in the retinal vascular microenvironment.

Function

The retinal vessels supply blood to the inner most 2/3 layer of the retina from the internal limiting membrane to the inner nuclear layer. Tight junctions located in the retinal capillary endothelial cells create a blood-retinal barrier.

Clinical Relevance

Many retinal pathologies are a result of disorders in the retinal circulation. Examples include diabetic retinopathy, retinal vascular occlusions, hypertensive retinopathy, sickle-cell retinopathy, and HIV retinopathy. Macular edema from retinal vascular dysfunction can also result from many different causes including diabetes, vein occlusions, radiation retinopathy, secondary to ocular surgery, uveitis, and hereditary retinal degenerations. Retinal vascular diseases also exist such as Coats' disease, juxtafoveal telangiectasias, and retinal arterial macroaneurysms. Inflammation of retinal blood

vessels, retinal vasculitis, can be associated with certain systemic diseases and types of uveitis.

Cross-References

- ▶ Carbonic Anhydrase Inhibitors, for Cystoid Macular Edema
- ▶ Central Retinal Vein, Occlusion of
- ▶ Coats' White Ring
- ▶ Diabetic Retinopathy
- ▶ Macular Edema
- ▶ Superior Ophthalmic Vein Thrombophlebitis
- ▶ Uveitis, Iridocyclitis

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Retinal Break

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Synonyms

Retinal tears

Definition

A full-thickness defect in the neurosensory retina

Etiology

Retinal breaks are full-thickness breaks that occur secondary to vitreous traction, more frequently at site of strong vitreal adhesion as a consequence of a posterior vitreous detachment (PVD), especially at the vitreous base. The posterior edge of the tear is its apex, and the anterior extensions are its base.

Lattice degeneration of the retina is another risk factor for the development of a retinal break. This is a condition in which peripheral retinal thinning is associated with liquefaction and separation of the overlying vitreous, associated with a pronounced vitreoretinal adhesion at the margin. When PVD occurs, traction at the margin of the lattice degeneration can lead to retinal tears.

Blunt trauma can also induce many varieties of retinal breaks, which include horseshoe tears, retinal dialysis, and macular holes. The major mechanism of peripheral break formation is hypothesized to be compression of the globe with subsequent distortion and expansion at the area of the ora serrata and equator. This expansion produces an acute increase in vitreoretinal traction, which often results in a retinal dialysis.

Horseshoe or flap tears with persistent traction often avulse the base of the tear to leave a small, round defect in the neural retina with an overlying operculum of retinal tissue. This generally indicates complete relief of vitreoretinal traction in this area.

Atrophic holes in the retina occur secondary to retinal thinning. Vitreous traction is not the pathogenic mechanism of atrophic retinal holes. Although these can occur in isolation, they often present within areas of lattice degeneration.

Open-globe injury with penetrating foreign body may cause retinal break immediately at the time of impact with two mechanisms: a direct retinal trauma, with disruption of the retina and necrotic breaks, or as result of latter vitreous traction. This retinal defects are typically irregular (Ryan 2013).

Clinical Presentation

Symptoms associated with acute horseshoe tears include floaters secondary to vitreous debris

(hemorrhage, retinal pigment epithelium cells) and flashes that result from persistent vitreous traction.

A significant visual loss could occur when retinal breaks are associated with vitreous hemorrhage.

Marfan's syndrome, Ehlers-Danlos syndrome, and homocystinuria can predispose to retinal break formation (Yanoff and Jay 2013).

Diagnosis

The diagnosis is typically clinical. A careful examination of the peripheral retina must be carried on by using a Goldmann three-mirror lens or with indirect ophthalmoscopy and scleral depression.

Differential Diagnosis

Pars plana cysts
Enclosed oral bays
Meridional folds/complex
Ora serrata pearls
Granular tags
Paving-stone degeneration
Chorioretinal scars
Peripheral cystoid degeneration
White with/without pressure
Retinal erosion

Prophylaxis

Upon the discovery of a retinal break, many factors should be considered: the presence or absence of symptoms; age and systemic health of the patient; refractive error of the eye; location, age, type, and size of the break; status of the fellow eye; and whether the patient is aphakic or pseudophakic or will soon undergo cataract surgery.

The presence or absence of symptoms in association with the onset of the break is the most important prognostic criterion for progression to retinal detachment.

In phakic patients who have no previous history of retinal disease or of high myopia and who develop *asymptomatic* horseshoe tears, atrophic holes, or holes with opercula, prophylactic treatment is rarely indicated.

Patients should be made aware of the symptoms of vitreous traction and retinal detachment and should be instructed on how to assess the peripheral visual field.

By contrast, in phakic patients, it is recommended that nearly all acute, *symptomatic* retinal breaks be treated to prevent retinal detachment.

Long-standing tears often have retinal pigment epithelial changes adjacent to them. These changes indicate to the clinician the decreased likelihood of retinal detachment; by contrast, supero-temporal breaks are more frequently associated with retinal detachment.

Retinal dialyses, whether traumatic or idiopathic, have a high association with the development of retinal detachment. In these cases, prophylaxis is usually indicated (Yanoff and Jay 2013).

Therapy

Aim of therapy is to provide a chorioretinal adhesion between the tear and the adjacent retina, which prevents liquid vitreous access through the hole and into the subretinal space. Most common first choice therapy is laser photocoagulation or cryotherapy.

Laser could be achieved indifferently with the argon green laser, krypton red laser, or diode laser, and it is delivered by slit lamp or indirect ophthalmoscopy. Slit lamp is preferred for posterior retinal break, while indirect ophthalmoscopic laser photocoagulation is preferred for anterior retinal breaks because of difficulty in treatment of the anterior margin at the slit lamp. The tear should be surrounded completely by three to four rows of laser burns. Although the spots need not be confluent, there should be no more than half a spot size of untreated retina between burns. Chorioretinal adhesion occurs the instant that the laser photocoagulation is applied, but maximal adhesion occurs 7–10 days later. Topical anesthesia alone is

enough in the majority of cases. If multiple large breaks are present and the patient is unable to tolerate the treatment, retrobulbar anesthesia may facilitate completion of the procedure.

Cryotherapy destroys the choriocapillaris, retinal pigment epithelium (RPE), and outer retina to provide a chorioretinal adhesion. One week is required to achieve partial adhesion and up to 3 weeks for the full adhesive effects to occur. Cryopexy can be delivered adequately despite the presence of extensive cataract, anterior or posterior capsular opacity, relatively dense vitreous hemorrhage, or anterior breaks. Transconjunctival cryotherapy under topical anesthesia (cotton-tipped applicators soaked in 4% lidocaine) is usually adequate. In some cases, 2% lidocaine injection subconjunctivally via a 30-gauge needle may be necessary. In eyes that fail prophylactic therapy, retinal detachment repair by pneumatic retinopexy, scleral buckling, or vitrectomy is usually successful in the anatomic reattachment of the retina (Kanski 2003; Ryan 2013; Yanoff and Jay 2013).

Prognosis

Failure rates for prophylactically treated retinal breaks depend on many factors, which include the type of retinal break, indications for treatment, length of follow-up, and definition of failure.

Risk factors for failure included aphakic or pseudophakic status, acute symptoms, retinal detachment in the fellow eye, and male gender.

Epiretinal membrane and macular pucker are other visually significant complications associated with prophylactic treatment of a retinal break; they occur in 1–5% of treated eyes. More rare complications that can occur include Adie's pupil, subretinal and vitreous hemorrhage, and breaks in Bruch's membrane. An exceedingly rare, but potentially devastating, complication in patients who have staphylomatous sclera and eyes treated with cryotherapy is scleral rupture (Ryan 2013).

Epidemiology

The incidence of retinal breaks at autopsy in individuals over 20 years of age is in the range 6–11%.

The annual incidence of retinal detachment is approximately 12 per 100,000 people per year.

The occurrence of retinal breaks increases with increasing age. Myopia is considered a risk factor for retinal breaks that lead to retinal detachment; however, prevalence of retinal breaks in myopic eyes is similar to that in eyes of general population (Ryan 2013).

Cross-References

- ▶ Retinal Peripheral Degeneration
- ▶ Retinal Detachment
- ▶ Retinal Detachment Rhegmatogenous

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Retinal Capillary Hemangioma

- ▶ Retinal Hemangioma

Retinal Cavernous Hemangioma

- ▶ Retinal Hemangioma

Retinal Coloboma

- ▶ Ectasia, Retinal

Retinal Concussion

► Commotio Retinae (Berlin Disease/Edema)

Retinal Contusion

► Commotio Retinae (Berlin Disease/Edema)

Retinal Detachment

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Synonyms

Ablatio retinae

Definition

Detachment of the neurosensory from the underlying retinal pigment epithelium.

Histology

Diagnosis of retinal detachment (RD) is usually made upon clinical or sonographical examination. Nevertheless, there are some specific changes found in histology. Like clinical findings, these depend highly upon stage of RD and are therefore dependent on time passed since acute RD.

At early stages, only little changes may be found within the retina. In animal models, the earliest sign is intraretinal edema. Photoreceptors show a loss of the horizontal orientation of the discs within the outer segment. Swelling of the nucleous may represent hypoxic condition of various retinal cells. Retinal pigment epithelium cells (RPE) present a swelling, and at later stages these cells partly separate from Bruch's membrane. Clumps of proliferating RPE cells and macrophages are later found on both surfaces of the detached retina.

At later stages, the detached retina shows signs of degeneration in outer retinal layers and general thinning. With more time passing, the retina shows changes with cell loss and large cystoid spaces at the inner and outer nuclear layer. In some cases persisting longer than 3 months, RPE cells proliferate at the junction of detached and attached retina.

As also can be found upon clinical examination, most retinal detachments develop proliferative vitreoretino pathy. This disease is characterized by sub-, epi-, or intraretinal formation of membranes. Upon histologic examination, hypocellular membranes can be found consisting of RPE cells, glia cells, and myofibrocytes – most likely dedifferentiated RPE cells. These cells produce collagen and other extracellular matrix (ECM) proteins. Among many others, transforming growth factor beta contributes to transformation of RPE cells and increased production of ECM proteins.

Immunohistochemistry

For diagnosis of RD, immunohistochemistry is of no relevance. However, for research, this technique is widely used as it allows detection of ECM proteins and constellation thereof in PVR.

Electron Microscopy

For diagnosis of RD, electron microscopy is of no relevance.

Molecular Diagnostics

There is no specific molecular diagnostics for RD. However, some syndromal genetic disorders are associated with increased incidence of RD (for example, stickler syndrome, FEVR).

Differential Diagnosis

RD – especially longstanding RD – may clinically be confounded with retinoschisis.

Cross-References

- ▶ Pars Plana Vitrectomy
- ▶ Retinal Detachment Rhegmatogenous
- ▶ Retinoschisis

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Retinal Detachment Rhegmatogenous

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Synonyms

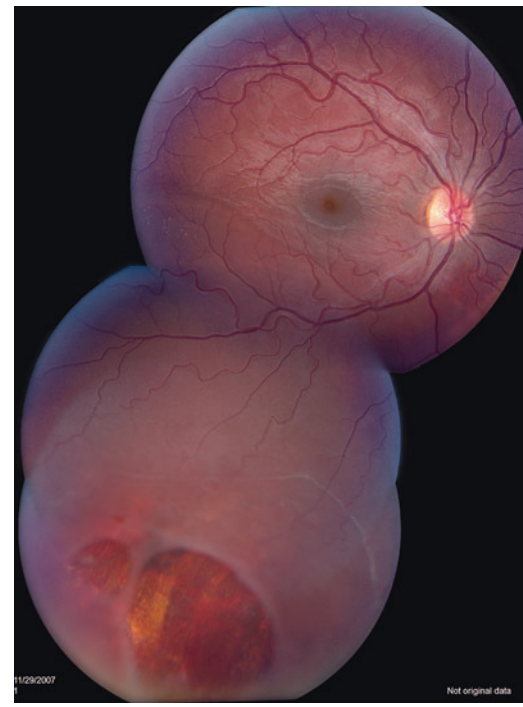
Retinal detachment

Definition

Detachment of the neurosensory retina from the underlying retinal pigment epithelium due to a full-thickness retinal break or breaks (Fig. 1).

Etiology

Rhegmatogenous retinal detachment (RRD) is caused by the passage of mobile, liquefied vitreous gel through a full-thickness retinal break, commonly a retinal tear, retinal hole, or retinal dialysis. It is generally agreed that vitreous traction must be present on or near the retinal break for rhegmatogenous retinal detachment to occur. Conditions that may be associated with rhegmatogenous retinal detachment include posterior vitreous detachment (PVD), trauma, high myopia, lattice degeneration, retinoschisis, infectious retinitis, uveitis, inherited vitreoretinal dystrophies, and prior history of retinal detachment.



Retinal Detachment Rhegmatogenous, Fig. 1 Inferior rhegmatogenous retinal detachment. Two adjacent retinal breaks are visible with bullous, subretinal fluid extending into the macula

Interventions associated with higher risk of rhegmatogenous retinal detachment include cataract extraction and Nd: YAG capsulotomy.

Rhegmatogenous retinal detachment may also be found in combination with tractional retinal detachment, which is characterized by vitreoretinal traction that mechanically detaches the neurosensory retina. Combined rhegmatogenous-tractional detachments may occur in patients with proliferative diabetic retinopathy, proliferative sickle cell retinopathy, proliferative vitreoretinopathy, and ocular trauma.

Clinical Presentation

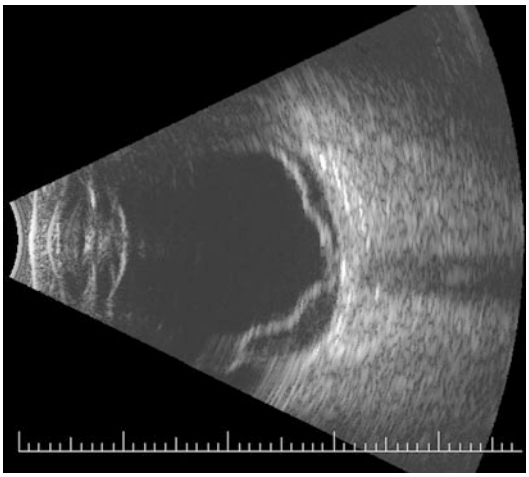
Patients may report symptoms of vitreoretinal traction and posterior vitreous detachment, including the sudden appearance of floaters and/or photopsias (flashes). Progressive accumulation of subretinal fluid ultimately results in a symptomatic visual field defect as more of the retina posterior to the equator is detached. Macular and particularly foveal involvement of the detachment results in central vision loss. Elevated intraocular pressure and inflammation may result, termed Schwartz-Matsuo syndrome.

Rhegmatogenous retinal detachment may be asymptomatic, however, when dissection of subretinal fluid is limited in area and the vitreous gel is less liquefied. Young, myopic patients with atrophic retinal holes or breaks associated with lattice degeneration without PVD, for example, may have subclinical detachments.

Diagnostics

Binocular indirect ophthalmoscopy with scleral depression remains the mainstay of diagnosis of rhegmatogenous retinal detachment and identification of causative retinal breaks.

When view of the fundus is obscured, B-scan ultrasonography (Fig. 2) can be used to characterize the location and extent of retinal detachment and to identify areas concerning for retinal break. Optical coherence tomography (OCT) may be used to confirm presence of subretinal fluid, particularly in cases when macular involvement may be in question, or to differentiate from retinoschisis.



Retinal Detachment Rhegmatogenous, Fig. 2 B-scan ultrasonography revealing retinal detachment. Shallow subretinal fluid is present superior and inferior to the optic nerve

Differential Diagnosis

Differential diagnosis includes tractional retinal detachment, exudative (serous) retinal detachment, and retinoschisis.

Prophylaxis

Prophylaxis targets prevention of the factors causing rhegmatogenous retinal detachment, namely: preventing passage of fluid vitreous through a full-thickness retinal break and/or relieving vitreoretinal traction.

Laser photocoagulation, cryotherapy, and far less commonly a scleral buckling procedure or vitrectomy may be used as prophylaxis of rhegmatogenous retinal detachment via prevention of fluid vitreous from passing through a retinal break (laser photocoagulation and cyrotherapy) or relief of vitreoretinal traction (scleral buckle or vitrectomy).

Treatment of symptomatic retinal tears, especially in the presence of posterior vitreous detachment, with laser photocoagulation or cryotherapy is recommended to prevent

rhegmatogenous retinal detachment. In regard to asymptomatic lesions or precursors of retinal tears, particularly atrophic retinal holes or lattice degeneration, data from prospective, randomized trials is unavailable to guide clinical practice. Prophylactic treatment of these asymptomatic lesions may be considered in high-risk patients such as those with vitreoretinal degenerations or a history of retinal detachment in the fellow eye. Patients should be counseled on symptoms of retinal traction or detachment, including photopsias, vitreous floaters, and visual field loss, and therapy should be individualized.

Therapy

Multiple options are available for treatment of rhegmatogenous retinal detachment. Comorbid ocular and systemic pathology, lens status, and surgeon preference may affect decisions regarding chosen method of repair.

Pars plana vitrectomy with intravitreal tamponade and scleral buckling procedure, used alone or in combination, are the mainstays of primary rhegmatogenous retinal detachment repair. Concurrent endolaser photocoagulation and cryotherapy are performed to seal retinal breaks. Injection of perfluorocarbon liquid, retinotomy/retinectomy, membrane peeling, and external or endo-drainage are surgical techniques that may be utilized to achieve anatomic reattachment.

In selected patients, pneumatic retinopexy and demarcation with laser photocoagulation or cryotherapy are appropriate office-based therapeutic approaches.

Prognosis

Visual acuity improves after successful retinal reattachment, but the degree of visual acuity may vary pending duration of detachment and involvement of the fovea. Failure of primary surgery, poor preoperative visual acuity, extensive detachment, and the presence of PVR have been associated with poorer visual outcome.

Single surgery anatomic success rates vary in prior reports but may be achieved in approximately 90% of patients, with final retinal reattachment achievable in approximately 95% of patients. Proliferative vitreoretinopathy is the most common cause of retinal detachment surgery failure and occurs in up to 10% of patients.

Epidemiology

The annual incidence of rhegmatogenous retinal detachment has been reported to be between 6.3 and 17.9 per 100,000 population, with a median incidence of 10.5 per 100,000 population. Risk of detachment in the fellow eye has been reported to be between 5% and 15%.

Cross-References

- ▶ Lattice Dystrophy
- ▶ Proliferative Endotheliopathy
- ▶ Posterior Vitreous Detachment
- ▶ Retinal Detachment
- ▶ Retinal Tears
- ▶ Tractional Retinal Detachment

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Retinal Hemangioblastomas

► Hemangioblastomas, with Retinal Angiomatosis (von Hippel Lindau Disease)

Retinal Hemangioma

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Synonyms

Retinal capillary hemangioma; Retinal cavernous hemangioma

Definition

Capillary hemangioma is a benign developmental tumor in which proliferating endothelial cells form a primitive capillary network usually fed by feeder vessels originating from the central retinal artery.

Cavernous hemangioma is a benign congenital collection of multiple thin-walled dilated vessels lined by non-fenestrated endothelium without feeder vessels (Singh et al. 2007).

Etiology

Capillary hemangioma results from a proliferation of endothelial cells, which is why some authors consider it a hemangioblastoma. In up to 60% of patients with either solitary or multiple retinal capillary hemangiomas, especially if there is a family history, there is association with von Hippel-Lindau (VHL) disease which has an autosomal dominant etiology.

Cavernous hemangioma could not be consistently linked with a systemic condition.

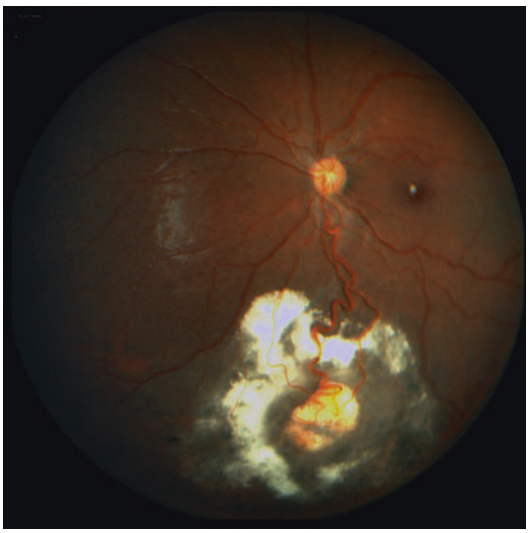
Clinical Presentation

Capillary hemangiomas can be detected by 25 years of age, when patients are screened due to a known VHL family history. In two-thirds of the cases, there is a red-orange intraretinal solitary lesion, while in one-third there are multiple lesions. In VHL, there may even be bilateral lesions. The lesions are usually found in the temporal periphery with feeder vessels or they may be found juxtapapillary without feeder vessels. The capillaries leak fluid causing exudative detachment and a decrease in the patients' visual acuity (Fig. 1).

Cavernous hemangiomas appear at any age from birth to 60 years of age. They can be solitary, but there are usually multiple grape-like blood-filled lesions appearing in the retina juxtapapillary area or over the optic nerve head. They usually do not leak fluid and thus do not cause a reduction in visual acuity.

Diagnostics

Clinical examination should be complemented by ultrasonography and fundus photography, along



Retinal Hemangioma, Fig. 1 Color fundus picture of a left eye with dilated tortuous vessels leading from the optic disk toward a typical peripheral retinal yellow lesion surrounded by subretinal fluid and white exudates

with optical coherence tomography (OCT) imaging. OCT can detect fluid accumulation resulting from leakage from the abnormal vessels within the hemangioma. Still, the most important imaging for these vascular lesions is fluorescein angiography. It can detect the feeder vessel leading from the disk to the capillary hemangioma and stain the exudation. OCT can detect both subretinal and intraretinal fluid. If the fluid does not extend into the central macular area, it should not cause a visual disturbance and can remain untreated.

Systemic correlations should be evaluated and may help in the diagnosis: VHL in patients with capillary hemangiomas. Patients with a cavernous hemangioma may have a similar brain lesion (a cerebral cavernous malformation).

Differential Diagnosis

Differential diagnosis includes ▶ malignant choroidal melanoma (amelanotic), ▶ Coats' disease, ▶ arterial macroaneurysm, ▶ and other vascular malformations.

Melanoma has a different ultrasonic internal reflectivity than hemangiomas, with medium-low internal reflectivity vs. high internal reflectivity, respectively. Coats' disease is usually diagnosed earlier in life and has telangiectatic vessels and significant exudation. Macroaneurysms are diagnosed later in life and are usually diagnosed after a bleeding event that results in blood under the retina, within the retina, and above it (preretinal hemorrhage and vitreal hemorrhage). There is no feeder vessel, but rather the macroaneurysm extends from a retinal arteriole. Lastly, vasoproliferative tumors do not have feeder vessels as do capillary hemangiomas.

Prophylaxis

There are currently no methods to avoid formation of retinal hemangiomas. However, patients with VHL disease should be followed carefully for early detection.

Therapy

Small non-leaking hemangiomas can be followed in cooperative patients. Photodynamic therapy has replaced laser photocoagulation in the treatment of capillary hemangiomas. Although more efficient in treating lesions smaller than 1.5 mm, when the lesions are more than 3 mm in diameter, one should use cryotherapy over laser photocoagulation. These larger lesions would also respond to brachytherapy. If a large lesion causes a retinal break, one should resort to vitreoretinal surgery in the treatment of the hemangioma.

Cavernous hemangiomas usually need no treatment as they do not progress. They may even spontaneously close with a thrombus. Other than a few reports of the use of laser photocoagulation, there is no known treatment for the retinal cavernous hemangiomas.

Prognosis

As a benign tumor, retinal hemangioma threatens patients' sight rather than their lives. A quarter of the patients will lose some of their vision permanently; a fifth retain only 20/100 in at least one eye.

Epidemiology

This is a rare condition with an unknown incidence.

Cross-References

- ▶ Arteriovenous Malformations (AVMs)
- ▶ Coats' White Ring
- ▶ Macroaneurysms
- ▶ Malignant Melanoma (MM)

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Retinal Hole

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Synonyms

Atrophic retinal holes; Atrophic retinal tears

Definition

Retinal holes are full-thickness breaks in the sensory retina not associated with vitreoretinal traction.

Etiology

Atrophic retinal holes are not caused by vitreoretinal traction, but atrophic changes in the sensory retina are supposed to be the main cause of these lesions. There appears to be no sex predilection.

Retinal holes are the result of chronic atrophy of the sensory retina. These lesions often take a round or oval shape. It has been postulated that the pathogenesis of this lesion stems from an atrophic pigmented chorioretinopathy that is associated with retinal vessel sclerosis and a disturbance of the overlying vitreous. As the blood supply to the retina is shut down, the retinal tissue subsequently dies in conjunction with degeneration of the surrounding vitreous. This pathology precludes traction of the vitreous to the underlying sensory retina.

Idiopathic atrophic retinal hole is the most common presentation. There are no generally accepted risk factors for this condition, but lesions have been cited more often in younger myopic patients. It has been estimated about 5% of the general population has atrophic holes. Atrophic holes often present in the peripheral (temporal or superior) retina.

Large, irregular retinal holes sometimes occur in an area of blunt impact (post-traumatic retinal holes) where there are fragmentation of the retina and hemorrhagic necrosis of the choroid.

Clinical Presentation

Retinal hole are full-thickness breaks in the sensory retina, round or oval in shape, with or without a perilesional subretinal fluid accumulation. Most rounds holes are solitary, although multiple holes may be present within a lattice lesion. Retinal holes are more common in myopic eyes, most often asymptomatic. They are usually detected during routine fundus examinations or in patients complaining of photopsia and myodesopsia due to other coexisting peripheral retinal lesions. Retinal holes can become symptomatic (photopsia) if a vitreoretinal traction acts on the edges of the lattice degeneration, which they are associated to. In post-traumatic retinal holes, portions of retina sometimes appear to be missing in the area of contusion, and these defects can be quite large. The irregular edges of large retinal breaks are frequently rolled, and pieces of necrotic retina may be present in the vitreous cavity overlying the irregular breaks. Small, atrophic retinal holes may appear later in areas of less severe commotion retinae.

Diagnosis

The diagnosis is typically clinical. A careful examination of the peripheral retina must be carried on by using a Goldmann three-mirror lens or with indirect ophthalmoscopy and scleral depression. In case of blunt trauma, a fundus examination must be repeated some days after the event, since retinal holes can develop late after trauma.

Differential Diagnosis

Horseshoe retinal tear, lattice degeneration, operculated retinal hole, snail track degeneration, and retinoschisis

Prophylaxis

Usually, in simple asymptomatic retinal holes, a prophylactic treatment is not required and a periodic fundus examination is recommended. Retinal hole with subretinal fluid, evidence of vitreoretinal traction on the edges of large areas of lattice degeneration in symptomatic patients, and history of retinal detachment in the fellow eye represent typical indications for a prophylactic argon laser photocoagulation.

Therapy

Therapy is rarely necessary.

Prognosis

Prognosis is good, with a low incidence of retinal detachment.

Epidemiology

Round atrophic retinal holes within areas of lattice degenerations are typically small measuring less than 0.3 mm. Round holes have been reported in 16–18% of lattice lesions in clinical studies. Atrophic holes within lattice lesions occur more frequently in older patients, and their prevalence increases in a linear fashion with increasing age to 43% at ages 50–59. The inferotemporal quadrant is the most common side of this retinal breaks. The clinical importance of atrophic holes is that they occasionally cause or contribute to retinal detachment.

Cross-References

- ▶ Retinal Break
- ▶ Retinal Detachment
- ▶ Retinal Detachment Rhegmatogenous
- ▶ Retinal Peripheral Degeneration

Further Reading

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Retinal Image Quality

▶ Image Quality, General

Retinal Migraine

▶ Retinal/Ocular Migraine

Retinal Peripheral Degeneration

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Synonyms

Some types of degenerations may have several names:

Microcystoid degeneration – Cystic retinal tuft; Paving stone degeneration – Cobblestone degeneration

Definition

A large family of pathologies, in which there is a degenerative process in one of the retinal layers of the anterior neuroretina or ora serrata. These pathologic processes may be grossly divided to three subfamilies:

1. Intraretinal degenerations which include the microcystoid degenerations, senile retinoschisis, and pars plana cysts
2. Retinovitreal degenerations which include the snail track degeneration, the lattice degeneration, and the white degeneration
3. Chorioretinal degeneration which include the paving stone degeneration

Etiology

The exact etiology of most of the peripheral retinal degenerations is not known. Most of the degenerations are due to aging, others are familial disorders, and some are associated with high myopia as lattice degeneration and snail track degeneration. Pars plana cysts may by associated in some cases with multiple myeloma or other diseases with abnormal protein production. White-without-pressure degeneration is considered to be a manifestation of peripheral vitreous traction.

Clinical Presentation

Intraretinal Degenerations

Microcystoid degeneration is characterized by small bubble-like lesions near the ora serrata. The lesions are visualized very well with scleral depression. They occur in the outer plexiform and inner nuclear layers of retina. Usually these degenerations are found in both eyes and more frequently are located in the supero-temporal quadrant of retina. Inner wall of the bubble may be absent, giving an impression similar to retinal hole, which is actually a pseudohole. The bubbles are filled with hyaluronidase-sensitive mucopolysaccharide. The reticular cystoid degeneration tends to occur in inner retinal layers and is located posterior and continuous with microcystoid degeneration in most of cases. It appears as linear or reticular lesions that follow the retinal blood vessels. Its histologic appearance is different from that of the microcystoid degeneration.

Expansion of both microcystoid and reticular degeneration may lead to senile retinoschisis, which is a bullous elevation of peripheral retina. It occurs mainly in the inferotemporal quadrant. It may be caused because of traction by zonular fibers or poor peripheral vascularization. Retinoschisis is usually asymptomatic and remains immobile with the eyeball movement. Sometimes it may produce an absolute field defect. With time it may enlarge toward the posterior pole, and further it may even lead to retinal detachment (RD). Retinoschisis may be classified into two subgroups: typical, which is a consequence of microcystoid degeneration, and reticular, which is a consequence of reticular degeneration. In the typical type, the retina splits in the outer plexiform layer. The inner retinal layers appear as smooth, oval lesions, whereas the outer layers are irregular and pockmarked with small "snowflakes-like" white dots, which may be seen on it. These dots represent the neurons and the Muller cells, which bridge or formerly bridged between the inner and the outer layers of the retina. In the reticular retinoschisis, the splitting occurs in the nerve fiber layer, and thus the inner, detached retinal layer is very thin and may be markedly elevated. Reticular degeneration is more prone to further RD than the typical one. The risk of RD remains rare nevertheless. Treatment is recommended only in the presence of holes in external layer.

Another type of intraretinal degeneration is the pars plana cysts. These cysts are clear, bullous elevations of nonpigmented ciliary epithelium of pars plana. They are usually seen underneath the temporal part of vitreous base. The cysts contain a clear fluid with high concentration of hyaluronic acid. In patients with multiple myeloma or other disease with abnormal protein production, an abnormal protein may accumulate in cysts that show a typical turbid appearance. These are harmless lesions not associated with serious eye complications.

Retinovitreal Degenerations

Snail track degeneration is a complex of shiny white dots, which may resemble salt grains.

These lesions are found in the area of or just in front of the equator. The pathological feature is an atrophy of retinal neural elements and deposition of lipids in the internal layers of retina. It is considered the early stage of lattice degeneration.

Lattice degeneration appears as one or several linear bands of thin retinal tissue at the equator of the eye. The lesion may be represented as fine white line or pigmentary changes within a band of retinal thinning. The bands may sometimes be traced to larger sclerosed or sheathed vessels. Histologically, there is an atrophy of the inner retinal layers and blood vessels with thick walls, which may accumulate irregular pigment. The overlying vitreous is liquefied, condensated, and adhered to the area of the margins of the degeneration process. In most cases, the degenerative area is covered with an internal limiting membrane, which protects it from RD. Actually, only 5–10% percent of patients with lattice degeneration will actually develop RD. These will be usually young patients with high myopia. Nevertheless, at eye examinations of patients with rhegmatogenous RD, lattice degeneration may be found in up to 30% of them. The tear will usually occur by means of traction of posterior or lateral margins of the lesion. In some cases, an atrophic hole in the middle of the lesion may be formed.

White degeneration is defined by white-appearing lesions of the peripheral retina. Some of such lesions are visualized with indirect ophthalmoscopy only and are called white degeneration without pressure. When retina appears normal without depression, but the white lesions are visualized with retinal indentation, these lesions are considered white-with-pressure degeneration. White-with-pressure degeneration has opalescent or milky white appearance. It may be found in 30–35% of normal eyes. Without depression, the retina appears absolutely normal. It is considered a benign condition, but the subclinical peripheral RD must be ruled out. White-without-pressure degeneration has a distinctive white color, which is brighter than the appearance of white-with-pressure degeneration. In this lesion, the choroid is almost absolutely obscured. If the sclera depression is performed, the whiteness is accentuated even more. The lesion borders are sharply demarcated. Some intervening areas of normal retina may be seen. These areas should not be confused with retinal holes. As in the white-with-pressure degeneration, the lesion may resemble RD, but after the indentation of the suspected area, it is clearly visualized that the retina is attached to the RPE. White with or without pressure presents no risk of retinal detachment. No treatment is recommended.

Chorioretinal Degeneration

Paving stone degeneration is a slowly progressive form of retinal degeneration, which is usually asymptomatic and do not lead to any complications, although it has a very dramatic appearance of multiple rounded punched-out lesions. They appear as patches of choroidal and retinal atrophy of half to several disc diameters. These lesions are located between the ora serrata and equator, in inferior quadrants of the retina. The color is yellow to white, which actually represents the sclera that lies just beneath the atrophic lesions. It is possible to see the choroidal blood vessels running through the base of the degenerative patch. The margins of the lesions are sharp and may be pigmented because of a surrounding rim of hypertrophic pigment epithelium. Several patches may merge and become confluent.

Diagnostics

The lesions are diagnosed with direct and indirect ophthalmoscopy. As it was mentioned before, parts of them have to be indentated for better visualization.

Differential Diagnosis

Retinoschisis has to be differentiated from the retinal detachment. In retinoschisis there is absolute scotoma. Usually there are no signs of

intraretinal hemorrhage or tobacco dust. The surface is very smooth and the detached layer appears thin and opaque. Underlying retinal pigment epithelium appears normal. In retinal detachment the scotoma is relative, "tobacco dust" and hemorrhages may be seen, and the surface will usually appear corrugated. If a pigmented demarcation line is present in the setting of retinoschisis, concomitant rhegmatogenous retinal detachment is present. Scleral depression is essential in distinguishing retinoschisis from retinal detachment. In contrast to retinal detachment, scleral indentation fails to collapse the cavity in retinoschisis.

Prophylaxis

Lattice degeneration is relatively common in general population (6–8%) and is prone to cause symptomatic tear with further RD in about 5–10% of patients with this lesion. Even though there is no indication for prophylactic treatment in a patient with incidental finding of lattice degeneration, in patients with lattice and risk factors for RD (the presence of a tear inside the lattice degeneration, retinal detachment in fellow eye, aphakia or pseudophakia, flap tears, future ocular surgery planned), preventive treatment may be indicated. Treatment is prophylactic laser retinopexy around the lesion. Although 6% of patients with RD have degenerative retinoschisis, for the vast majority of patients with this degeneration, there is no indication for prophylactic treatment, and the natural course of this lesion is to remain stable over years. Retinoschisis is treated if it is symptomatic or progressive and if threatens the macula. Laser demarcation of retinoschisis or treatment of margins of outer retinal layer breaks should be avoided.

Although microcystoid degenerations present some risk for development of RD, being associated with posterior vitreous detachment, these lesions are not recommended for prophylactic treatment in otherwise healthy eyes.

Prophylactic treatment of the fellow eye is doubtful in most types of degenerations. Although some of the patients who developed RD in one eye as a complication of degenerative process are in increased risk for RD in the fellow eye, there are not sufficient prospective, evidence-based studies to show that prophylactic treatment of the fellow eye will actually prevent RD. In lattice degeneration there are only some indications for preventive laser treatment of the fellow eye, but studies showed a modest treatment benefit. Current indications for prophylactic intervention are poor surgical results in the first affected eye and treatment of patients unable to recognize symptoms of RD and of patients who live in areas with limited access to ophthalmologic care. Myopic patients with atrophic holes in lattice lesions have to be evaluated periodically. During the evaluation, they have to be counseled about loss of peripheral vision, because slowly progressive retinal detachments can occur. In patients with degenerative retinoschisis and RD in one eye, there is no absolute indication for prophylactic treatment of the fellow eye. The prophylactic treatment is indicated only for unusual cases, in which breaks in outer layer of retina are responsible for retinal detachment in the first eye, while outer layer breaks and retinoschisis are present in the fellow eye.

Treatment

Treatment of degenerative processes is usually designed to prevent RD, and thus only lesions with appropriate prophylactic indications are treated. The main treatment techniques are laser photocoagulation and cryotherapy. Laser treatment is very effective for more posterior lesions, the greatest advantage of this procedure being an almost immediate effect on the tissue with proper visualization (by laser burns) of the already treated area. During the procedure, the margins of the degenerative lesion are demarcated with laser-applied burns. Eyes with small pupil or variable media opacities (e.g., partial cataract, mild vitreous hemorrhage) are not good candidates for this treatment. Cryotherapy is very effective in treating especially anterior

lesions farther located and of eyes with partial opacities of the ocular media, such as mild vitreous hemorrhages and cataract. During this procedure, cold burns are applied on or near the lesion area (depending on the lesion size), using a cryoprobe applied from the outer sclera side of the eye. One of the main disadvantages of this technique is the limited visualization of already treated areas during the procedure, since the effect of the cold burn is visualized only after several days.

Prognosis

Most degenerative lesions remain stable over time. However, some types may render the patients' eyes at higher risk for retinal breaks and further on for rhegmatogenous retinal detachment.

Microcystoid and paving stone degenerations usually do not predispose to retinal detachment. Most cases of retinoschisis are asymptomatic and nonprogressive over years. Snail track degeneration and lattice degeneration commonly lead to the development of retinal holes and in up to 10–20% of cases may lead to RD.

Epidemiology

Peripheral cystoid degeneration is present in almost all individuals over 20 years of age. Paving stone degeneration is very common, occurring in up to 22% of adult eyes, and it is bilateral in 30% of cases. Lattice degeneration is not a rare form of peripheral retinal degeneration. Its prevalence is about 10% of the general population and may be bilateral in 50%. Pars plana cysts are seen in 5–10% of general population, affecting both genders. The cysts are bilateral in 1/3 of cases. Senile retinoschisis occurs in 2–4% of population above age of 40 years. Snail track degeneration is more typical in young patients.

The incidence of white-with-pressure degeneration as well of paving stone degeneration increases with age.

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Retinal Pigment Epithelium

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Synonyms

RPE

Definition

RPE is one of the layers of retina formed by epithelial cells of neuroectodermal origin. The cells are hexagonally or cuboidally shaped cells which contain pigment. This single cuboidal epithelium layer is situated at the outer segments of the retina between the photoreceptors, at their apical part, and Bruch's membrane at their basal part. It extends from the margin of the optic disc to the ora serrata and is continuous with the pigment epithelium of the ciliary body. RPE cells play an important role in retinal function.

Structure

The apical portion of the RPE has villous processes that envelop the basal part of the photoreceptor cells. RPE are short, cuboidal cells, with a diameter at the periphery of about 16 μm. Macular RPE cells are much more dense and taller. In the area of fovea, RPE cell density is highest. Lateral surfaces of adjacent epithelial cells are closely

joined with each other by junctional complexes (tight junctions) and the adherens junctions. These junctional complexes form the outer blood-retinal barrier (BRB) and contribute to the RPE layer integrity and stability. The basal surface of the cells shows a rich enfolding of the plasma membrane. This surface is firmly attached to its basement membrane – the innermost layer of Bruch's membrane. RPE cells contain high amount of melanin-rich granules. These granules contribute to the typical brownish appearance of the fundus. The highest concentration of the pigment is found in the peripheral retina, while the lowest in the area of the macula.

The RPE is represented by two highly reflective lines in the optical coherence tomography (OCT) images: the Verhoeff's membrane, also called in the new terminology "interdigitation zone" (where the tips of the cone photoreceptor outer segments are enveloped by microvilli) and the RPE/Bruch's complex.

Function

The RPE cells perform essential functions:

- Absorb light
- Provide phagocytosis of the shed photoreceptor membranes
- Ensure retinol metabolism
- Form the outer BRB
- Ensure retinal attachment
- Transport nutrients to photoreceptors
- Heal and form scar tissue
- Perform an immune function

Light absorption: Each RPE cell has number of melanosomes – cell particles with melanin molecules distributed on protein fibers – that are located at the apical portion of the RPE. Melanin is a biologic light absorber, which is able to react differently on light according to variations in wavelength. Blue light with shorter wavelength is absorbed much more than red light with longer wavelength (Rayleigh absorption). Proper light absorption is important for the formation of better image as received by the retina.

Phagocytosis: RPE cells are macroglia, and as such, they continuously ingest debris from photoreceptors, cell membranes, cell discs, and other shed cell segments. Each RPE cell provides "cleaning services" to about 30–45 photoreceptors. The waste material is processed by certain phagocytized enzymes located within the RPE cells lysosomes. RPE dysfunction is supposed to explain the formation of drusen, an extracellular, amorphous deposit of material on Bruch's membrane in the macula.

Retinol metabolism: Retinal and polyunsaturated fatty acids are found in the outer segment discs. These acids play an important role in photoreceptors function and the visual cycle, thus have to be recycled. II-cis-retinaldehyde is reduced to the II-trans-retinaldehyde during the reaction with light in the photoreceptors. Most of the steps of regeneration to the II-cis configuration occur in the RPE.

Form the outer BRB: The blood-retina barrier prevents diffusion of metabolites between the choroid and the subretinal space and so contributes to the separation of the neurosensory retina from the outer environment. The RPE cells are important for the regulation of the photoreceptors' environment. This regulation is done by proper control of molecules and proteins that cross the BRB. RPE barrier functions by the way of two major components, the tight junctions and the polarized distribution of the RPE membrane proteins. Tight junctions are dynamic structures that can modify the BRB permeability by different physiological and pharmacological conditions. One of the important functions of the RPE is to "dehydrate" the inner layers of retina. These cells are capable to pump out water molecules and so prevent the formation of edema in neurosensory retina.

Retinal attachment: Dehydration of the inner retinal layers contributes to the close attachment of the photoreceptors to the RPE. Apical expression of neural cell adhesion molecules (N-CAM) by the RPE cells helps as well to keep the integrity between the neural retina and the RPE. Separation of the retinal outer segments from the RPE may lead to decreased phagocytosis and consequently accumulation of outer segments in the subretinal space.

Nutrient transport: Different pumps, transporters, and cotransporters are located on the apical and basolateral membrane surfaces. These, together with close control of the tight junctions, contribute to selective transport of nutrients, ions, and other molecules to the neural retina.

Heal and form scar tissue: External stimuli may cause trauma or inflammation of the retina. RPE have an important role in the healing process. Epithelial cells are able to proliferate, migrate, and transform to macrophages and fibroblast-like cells, and so they are contributing to the healing of the damaged tissue. Unfortunately, this property of the RPE sometimes contributes to pathologic processes of the retina. For instance, hypoxia-enhanced production of vascular endothelial growth factors (VEGF) by the transformed RPE cells may play a role in induction of choroidal neovascularization. Enhanced collagen production may cause a contraction of cellular retinal membranes and so lead to retinal detachment.

Immune function: As a crucial part of the BRB, RPE cells have an important role in the regulation of local immune response. In the presence of the inflammatory response, RPE may inhibit the action of inflammatory mediators. RPE cells secrete the tumor necrosis factor α (TNF α) receptors, which inhibit the action of proinflammatory TNF α molecule. They are also able to suppress the neutrophil superoxide generation, thus limiting tissue injury during inflammation. Breakdown of the BRB may initiate T cell activation with signaling through RPE cells, resulting in non-antigen specific lymphocytic infiltration. These epithelial cells have an important role in the synthesis of many immune modulating molecules and immunomodulatory cytokines and so control the local immune reaction of T cells and other immune system components.

Clinical Relevance

RPE has an important role in regulation of different processes in the retina. Any RPE anomaly may cause retinal pathology.

Hypertrophy of the RPE cells may result from a variety of causes, including trauma. Congenital hypertrophy of the RPE (CHRPE) produces slate gray-black flat lesions, usually in the periphery of the retina. These lesions often have depigmented lacunae, particularly in older individuals, and are often surrounded by a depigmented halo.

Hyperplasia of the RPE may contribute to epiretinal membrane (ERM) formation following rhegmatogenous retinal detachment.

RPE degeneration and atrophy play an important role in the pathogenesis of age-related macular degeneration (AMD).

In Best vitelliform dystrophy, the mutation in the Best1 gene causes production of a novel, transmembrane chloride channel at the basolateral plasma membrane of the RPE. It causes abnormal ion flux and subsequently accumulation of lipofuscin at the basal part of RPE. This lipofuscin accumulation contributes to the typical yellow, yolk-like macular lesion.

Albinism is a congenital disorder of melanin production. It is associated with decreased vision, photophobia, and nystagmus.

Cross-References

- ▶ Bruch's Membrane
- ▶ Neurosensory Retinal Detachment
- ▶ Photoreceptor Cells

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Retinal Tears

- ▶ Retinal Break

Retinal/Ocular Migraine

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Synonyms

Ocular migraine; Ophthalmic migraine; Retinal migraine; Visual migraine

Definition

Retinal migraines (more properly retinal vasospasm) were defined in 1988 by the International Headache Society (IHS) as at least two attacks of fully reversible, transient monocular visual loss or disturbances associated with migraine headache. The complete diagnostic definition, as outlined by the IHS is detailed in the "Diagnostics" section below. However, recent literature challenges the notion that monocular visual loss is physiologically associated with migraine headaches. Instead, some researchers propose that "presumed retinal vasospasm" with or without associated migraine would be a more accurate diagnosis for most patients.

Etiology

The pathophysiology of retinal migraine/vasospasm remains controversial. The two main criteria are monocular visual disturbance and migraine headache. Some cases of retinal vasospasm however do not have the migraine headache (acephalgic migraine equivalent). Proposed causes of migraine headache related neurologic deficit including visual loss include spreading depression or vasospasm. Retinal vasospasm is the predominant theory for "retinal migraine," and the cortical spreading depression in bilateral migraine aura would be difficult to prove in the human retina causing monocular visual loss.

Clinical Presentation

Patients with retinal migraine/retinal vasospasm typically present after rather than during the visual symptoms. Rare patients with transient retinal vasospasm has been imaged and photographed. Unfortunately, some patients may have difficulty defining strictly monocular versus bilateral visual defects which can make the diagnosis more difficult. Typical migraine associated with aura (bilateral) is more common than monocular retinal migraine/vasospasm.

Diagnostics

Retinal migraine/vasospasm is generally considered to be a diagnosis of exclusion. The diagnostic criteria for a retinal migraine are strictly defined by the IHS as:

(A) At least two attacks fulfilling criteria **B** and **C.**
(B) Fully reversible monocular positive and/or negative visual phenomena (scintillations, scotomata, or blindness) confirmed by examination during an attack or (after proper

instruction) by the patient's drawing of a monocular field defect during an attack.

(C) Headache, fulfilling the following criteria for a "migraine without aura" begins during the visual symptoms or follows them within 60 min.
- Headache attacks lasting 4–72 h (untreated or unsuccessfully treated).
- Headache has at least two of the following characteristics:
  - Unilateral location, pulsating quality, moderate or severe intensity, aggravation by or causing avoidance of routine physical activity
- During headache at least one of the following:
  Nausea/vomiting or photophobia/phonophobia

(D) *Normal ophthalmologic examination between attacks.*

(E) *Not attributed to another disorder (other causes of monocular vision loss excluded).*

Differential Diagnosis

The monocular manifestation of visual disturbances in retinal migraines is the primary characteristic which distinguishes this rare condition from several other types of migraines associated with aura visual disturbances (e.g., familial/sporadic hemiplegic migraine, basilar-type migraine). Aura, believed to be caused by spreading depression in the occipital cortex, typically affects a visual hemifield and is thus bilateral in nature. Transient ischemia from other etiologies should be considered in the differential diagnosis (e.g., thrombosis, emboli, vasculitis).

Prophylaxis

Identifying and avoiding environmental triggers such as stress and sleep deprivation is one method of reducing subsequent migraines. Upon initiation of visual symptoms, patients may try to abort the event by the use of nonsteroidal anti-inflammatory drugs (NSAIDs).

Therapy

Little data exists to guide effective treatment of retinal migraines. Migraine treatments are often tailored to what is most effective on a patient by patient basis. Historically, effective treatments have included aspirin, other NSAIDS, and some epilepsy drugs. Prophylactic therapy with tricyclic antidepressants, beta-blockers, and calcium channel blockers has also been advocated with variable success.

Prognosis

Variable depending on severity and frequency of attacks.

Epidemiology

True retinal migraine/vasospasm as defined by the IHS criteria is probably rare. In a review of reported cases, it was asserted that the frequency of retinal migraines has been historically overstated as most of the diagnosed patients do not meet the full IHS criteria.

Cross-References

► Ophthalmic Migraine
► Visual Migraine

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Retinitis

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Definition

Retinitis is an inflammation of the retina, most commonly related either to an infectious or an inflammatory cause. It is a nonspecific sign that accompanies many diverse causes of ocular inflammation and indicates the inflammation is involving the retina, either in isolation or in association with other structures, such as the choroid (chorioretinitis) or the optic nerve (neuroretinitis).

Etiology

Retinitis has inflammatory and infectious causes, which are either parasites, bacteria, viruses, or fungi.

The most common cause of infectious retinitis is related to *Toxoplasma gondii* which is an obligate intracellular protozoan parasite. Ocular toxoplasmosis may be congenital due to transplacental transmission of tachyzoites or acquired following consumption of raw or undercooked meat containing cysts or by ingestion of fruits, vegetables, or water contaminated by cat feces rich in oocysts. Other parasites that may can cause retinitis include toxocariasis, onchocerciasis, and diffuse unilateral subacute neuroretinitis can be caused by several different parasites.

Cytomegalovirus (CMV) retinitis is seen predominantly in immunocompromised patients and especially those with acquired immunodeficiency syndrome (AIDS). It may also occur following organ transplantation in patients receiving systemic immunosuppression or following chemotherapy for malignant disease. Following a primary CMV infection, which is usually asymptomatic in immunocompetent people, the virus remains latent and only reactivates when the immune system is suppressed.

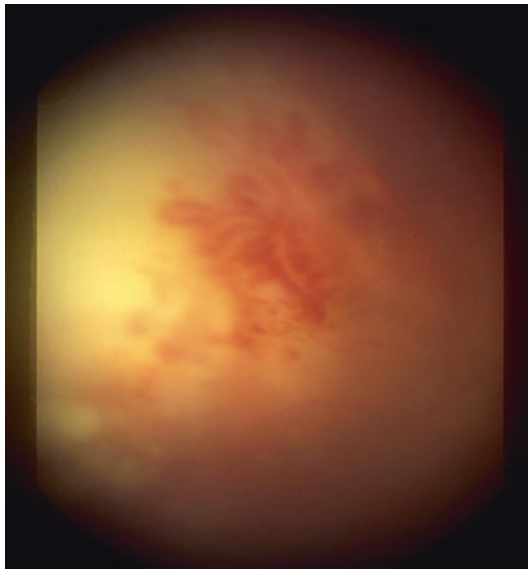
Acute retinal necrosis (ARN) is caused by herpes simplex or varicella zoster virus (VZV) infections. In immunocompetent patients these viruses result in a progressive peripheral necrotizing retinitis. In immunocompromised patients infections can cause a rapidly progressive disease, progressive outer retinal necrosis (PORN), which can involve the posterior pole and has a very poor visual prognosis.

Noninfectious retinitis can be related to systemic diseases such as Behçet disease and sarcoidosis.

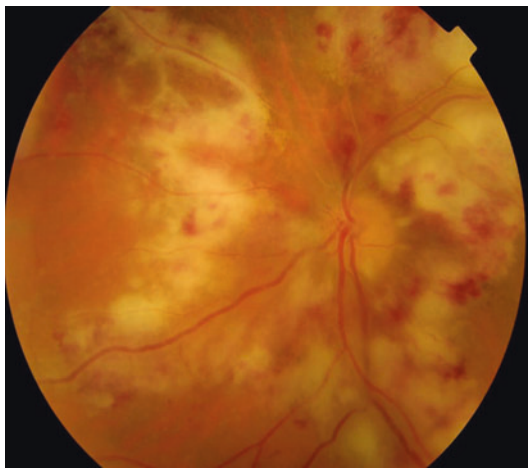
Clinical Presentation

Retinitis manifests as either focal or diffuse areas of pale-white retina accompanied by retinal hemorrhages, vascular sheathing, retinal ischemia, and retinal necrosis. In ARN, lesions are white yellow, small, and multifocal located in the peripheral retina which progressively enlarge and coalesce spreading circumferentially toward the posterior pole (Fig. 1). In PORN at the time of diagnosis, the retinitis may already involve the posterior pole and is rapidly progressive, leading to severe vision loss in most cases.

In CMV retinitis, the lesions are white and granular in appearance and may be surrounded by retinal hemorrhages. Because CMV retinitis occurs in immunocompromised patients, there is little vitritis, even in the presence of extensive retinal involvement. Progression of the lesions is slow and in a characteristic "brushfire" pattern, resulting in atrophic retina behind the active edge (Fig. 2). Toxoplasma retinitis occurs either in primary disease or adjacent to an existing scar in disease reactivation (Fig. 3). In primary infection, retinitis appears as a white, raised area with

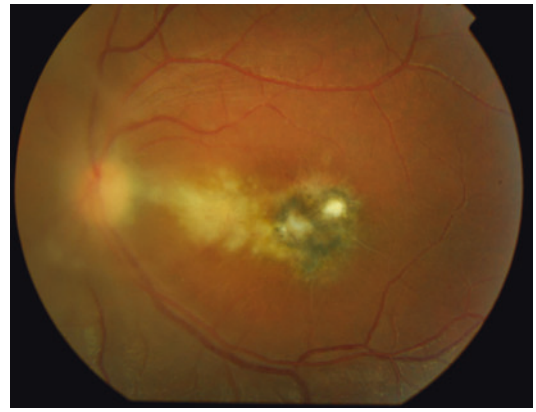


Retinitis, Fig. 1 Patient with VZV-related ARN with peripheral necrotizing retinitis

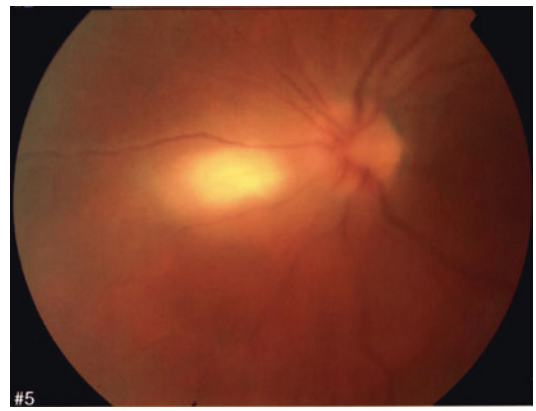


Retinitis, Fig. 2 Retinal image of an HIV patient with CMV retinitis. Note the extensive involvement of the posterior pole with widespread retinal hemorrhages and the brush border

indistinct borders (Fig. 4) and may involve nearby retinal vessels resulting in retinal artery or vein occlusion. Retinitis in Behçet disease is ischemic in type, can be isolated or multifocal, and usually occurs with significant vitritis (Fig. 5).



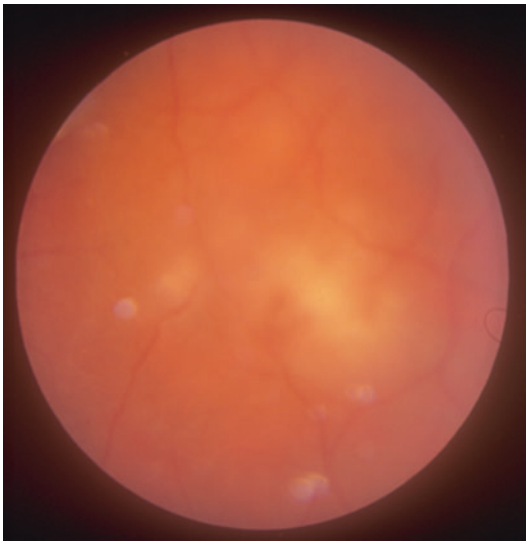
Retinitis, Fig. 3 Toxoplasmic reactivation at the border of an old pigmented chorioretinal scar



Retinitis, Fig. 4 Primary toxoplasmosis causing retinitis near the optic disk

Diagnosis

As retinitis is a nonspecific sign related to many conditions, a detailed history and clinical examination are important in guiding the diagnostic work-up, particularly with regard to infectious etiologies. Retinal imaging tests, such as fluorescein angiography, may be helpful in identifying the extent of retinal involvement and areas of retinal ischemia. Depending on the clinical presentation, systemic work-up, including blood tests, may be warranted. Table 1 lists the recommended systemic investigations in cases of retinitis. In cases when a viral cause is suspected, a vitreous biopsy should be obtained



Retinitis, Fig. 5 Patient with Behçet disease with a patch of retinitis associated with vitritis

Retinitis, Table 1 Recommended systemic investigations to identify etiology of retinitis

Etiology	Systemic investigations in retinitis
Sarcoidosis	Serum angiotensin-converting enzyme (ACE), chest X-ray
Syphilis	Specific treponemal (FTA-ABS) and nonspecific treponemal antibody (VDRL)
Toxoplasmosis	Toxoplasma serology
Cat scratch disease	Bartonella serology
HIV infection	HIV serology
Behçet disease	HLA-B51
Birdshot chorioretinopathy	HLA-A29
Tuberculosis	Interferon-gamma release assay (QuantiFERON Gold, Mantoux, or T-spot tests), chest X-ray

and polymerase chain reaction (PCR) testing performed for the presence of viral deoxyribonucleic acid (DNA).

Differential Diagnosis

In most cases the clinical appearance and history can direct the investigations to identify the etiology (Davis 2012). Other retinal lesions that should be distinguished from retinitis include cotton-wool spots, related to infarcts of the retinal nerve fiber layer and hard exudates. In cases of immunosuppressed patients, the clinical appearance may be atypical, and accompanying signs such as vitritis and anterior chamber reaction may be missing. Masquerade syndromes, for example, malignancy, should be considered in the presence of systemic involvement or if the ophthalmic signs are atypical.

Therapy

Cases of inflammatory retinitis are treated with local or systemic immunosuppressive therapy. Corticosteroids are the mainstay of systemic treatment, with the addition of second-line immunosuppressive agents as required. Local treatment is also predominantly corticosteroid-based and may be administered in the form of periocular or intravitreal injections or longer-acting intraocular implants.

Sight-threatening infectious retinitis must be treated promptly with appropriate antimicrobial therapy. In all cases of a suspected infectious cause, antimicrobial treatment must be given with the steroid treatment, and local steroid injections should not be used.

Not all cases of toxoplasmosis in immunocompetent individuals require treatment as the disease is self-limiting. Treatment should be given in cases of immunocompromised patients or when vital retinal structures are involved such as the fovea, optic disk, or main blood vessels. There are several treatment regimens including: (1) sulfadiazine and pyrimethamine together with folinic acid to reduce the bone marrow toxicity of pyrimethamine, (2) trimethoprim-sulfamethoxazole (co-trimoxazole), and (3) clindamycin in cases of individuals with allergies to sulfur-containing drugs (Harrell and Carvounis 2014). High-dose prednisolone is usually given with the antibiotic therapy to reduce the inflammation.

In cases of CMV retinitis, oral or intravenous ganciclovir or intravenous foscarnet may be used

initially in induction doses for 2–3 weeks followed by long-term maintenance therapy. Foscarnet or ganciclovir can also be administered intravitreally (Huynh et al. 2011). The underlying cause of immunodeficiency, for example, HIV infection, should be managed in conjunction with other physicians.

ARN is commonly treated using intravenous aciclovir for 7–10 days, followed by oral aciclovir for 6–12 weeks. Alternatively, oral valaciclovir for 6 weeks may be used. Systemic steroids may be used in immunocompetent patients to help control the inflammation. In the case of immunosuppressed or immunodeficient patients, management of disease in close liaison with other physicians is advised, and steroids are contraindicated (Wong et al. 2013). Following resolution of the acute inflammation, areas of extensive retinal necrosis are at a high risk of developing retinal tears and retinal detachments. These are related to posterior vitreous detachments that happen following the extensive vitritis in these cases and typically occur within the first 6 weeks after the beginning of the retinitis. Barrier laser to try and prevent any retinal detachment affecting the posterior pole may be considered. In cases of non-clearing dense vitreous opacities, vitrectomy may be required several months later when the eye is quiet (non-inflamed). For retinal detachment, vitrectomy surgery with silicon oil tamponade is usually required.

Prognosis

The prognosis of retinitis depends on the etiology, the visual acuity at the time treatment is started, the degree of involvement of the macula and the optic disk, and the development of subsequent complications, such as retinal detachment.

In cases of noninfectious retinitis, prompt treatment and long-term immunosuppressive control of the disease result in a stable long-term visual outcome, with most patients maintaining the vision at presentation. Causes of vision loss include macular scarring and atrophy, chronic cystoid macular edema, epiretinal membranes, and macular ischemia (Tomkins-Netzer et al. 2014).

In cases of ARN, the extensive retinal necrosis can lead to the development of retinal detachment, posterior pole involvement, and vitreous hemorrhages, all of which result in a poor long-term visual outcome (Wong et al. 2013). In CMV retinitis, treatment is effective in arresting the progression of retinitis and minimizing the complications related to that. Anti-retroviral therapy is required to control CMV replication in the long term and prevent further recurrence. However, patients may develop significant visual impairment secondary to large areas of retinal involvement, recurrent disease, epiretinal membranes, cystoid macular edema, cataract, or retinal detachment.

In toxoplasmosis, the visual prognosis depends on the location of the retinal involvement. Posterior pole involvement in the form of macular scars, optic nerve involvement, or vascular occlusion can lead to severe vision loss.

Cross-References

- ▶ Acute Retinal Necrosis (Necrotizing Herpetic Retinitis)
- ▶ Birdshot Retinochoroidopathy (Vitiliginous Chorioretinitis)

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Retinitis Pigmentosa, Decreased Vision in Neuro-Ophthalmology

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Synonyms

Primary pigmentary retinal degeneration; Progressive pigmentary retinopathy; Rod-cone dystrophy

Definition

Retinitis pigmentosa (RP) is a class of genetic degenerative retinal disorders that affect the photoreceptor cells (rods and cones) as well as the retinal pigment epithelium. Over 35 different genes have been identified, and modes of inheritance for RP include autosomal recessive, autosomal dominant, and X-linked transmission. This family of disorders typically results in painless, bilateral, and progressive vision loss due to dysfunction and eventual atrophy of rods, cones, and retinal tissue. Disease onset and manifestation of symptoms can be highly variable as a wide number of hereditary abnormalities can result in RP. In most cases appreciable deficits develop over the course of 1–3 years. The severity and patterning of visual dysfunction is dependent on the distribution of cell and tissue damage, but loss of vision is irreversible.

Nyctalopia

Loss of night vision or night blindness (nyctalopia) is a cardinal sign of RP and results from a progressive loss of light-sensitive rod cells. Rod cells function in the detection of objects and movements in low-light settings and are found throughout the retina with the exception of the macula. Patients with RP generally lose rod cells first, thus loss of night vision is often the first clinical sign of disease. Night blindness is not a symptom exclusive to RP and can also be seen in other retinal disorders, myopia, and age-related macular degeneration. In RP, night blindness usually manifests in the first one to two decades of life. Earlier onset of night blindness has been linked to autosomal recessive disease types, while later onset is often seen in autosomal dominant modes of inheritance.

Visual Field Defects

Patients with RP will experience a peripheral narrowing of the visual field over time due to the loss of rod function. As with the deficits in night vision, visual field defects also usually manifest in early adolescence. Earlier onset has been linked to increased disease severity. Defects are usually seen first in the superior visual field, suggesting damage occurs initially in the inferior portion of the retina. Patients may not initially detect these changes, but appreciable deficits are seen over the course of years or decades. In some cases, visual fields may be altered within months; however, with central vision intact, these more drastic changes can go unnoticed by the patient.

Central acuity is usually maintained until middle age (age 40–50). In less severe forms of disease, central visual acuity can be preserved

beyond age 60 or can be retained for all of a patient's life. Peripheral vision is usually lost first in RP; however, loss of central acuity is not uncommon and can occur during early stages of disease. Cases with loss of central acuity before peripheral loss are referred to as "inverse retinitis pigmentosa" and are usually found in older patients. Defects in central acuity result from damage to the fovea of the retina. This can be caused by damage to the retinal pigment epithelium localized to the fovea, retinal vascular leakage, or cystoid macular edema.

Cone cells, responsible for high visual acuity and color vision, are initially maintained in RP. Most patients do not report difficulty with differentiating colors. Cone cells are highly concentrated in the fovea; damage to the fovea results in deficits in color vision as well as sensitivity to bright sunlight.

Diagnostic Findings

On fundoscopic exam, retinitis pigmentosa is characterized by the presence of retinal pigment epithelium changes (bone spicules). The amount of bone spicules is variable among patients and may be less prominent in young children. Thinning of the retinal pigment epithelium (RPE) and a loss of photoreceptor cells can be detected using fundus autofluorescence and optical coherence tomography (OCT). Other ocular manifestations of the disease include optic nerve gliosis, loss of choriocapillaries, and attenuation of retinal arterioles. The extent of these findings, including the amount of pigment and degree of optic nerve gliosis, increases with age. In RP, electroretinography (ERG) may also indicate loss of photoreceptor cell function. Some patients with RP have optic disk drusen that can mimic papilledema or can have waxy pallor of the optic disk.

Prognosis and Treatment

Retinitis pigmentosa is characterized by deficits in night vision and visual fields that progress over the course of 1–3 years. The progressive loss of rod and cone cells results in these irreversible defects, and although uncommon, complete blindness can occur.

There is currently no proven effective treatment for retinitis pigmentosa; however, there are some therapies that have been suggested to alleviate associated symptoms. Oral acetazolamide may be used to treat cystoid macular edema. Many causative genes have been identified in RP, and gene therapy clinical trials are under investigation. Patients with RP are advised to take vitamin A supplements and use UV-protective eyewear.

Cross-References

- ▶ Atypical Retinitis Pigmentosa (RP)
- ▶ Electroretinogram
- ▶ Nyctalopia: Night Blindness
- ▶ Tunneling

Further Reading

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Retinitis Punctata Albescens

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Synonyms

Atypical retinitis pigmentosa (RP)

Definition

Variant of retinitis pigmentosa characterized by numerous punctate whitish-yellow flecks at the level of the retinal pigment epithelium.

Etiology

Although the exact etiology of retinitis punctata albescens remains unclear, studies suggest the pathogenesis involves an abnormal RLBP1 gene. This gene encodes cellular retinaldehyde-binding protein (CRALBP), which is vital to the normal cycling between all-trans retinal and 11-cis-retinol. Dysfunction of this protein leads to the characteristics symptoms of the disease (Carr and Noble 1999; Gass 1997; Weleber and Gregory-Evans 2006).

Clinical Presentation

Similar to patients with retinitis pigmentosa, patients with retinitis punctata albescens present with night blindness, peripheral visual field loss, photopsias, and decreased central visual acuity. Fundus exam demonstrates numerous whitish-yellow flecks at the level of the retinal pigment epithelium which extend in a radial pattern, are most prominent at the equator, and typically spare the macula. Retinal changes also often include the typical findings of retinitis pigmentosa, including attenuation of the retinal arterioles, waxy pallor of the optic nerve, and peripheral bone-spicule formation.

Diagnostics

The diagnosis of retinitis punctata albescens begins with a thorough history, inquiring about any night blindness, peripheral visual field loss, photopsias, and central visual acuity loss. Slit lamp biomicroscopy should investigate the presence of subcapsular cataracts, waxy or pale optic nerves, attenuated retinal arterioles, or any whitish-yellow flecks at the level of the retinal pigment epithelium. Formal visual field testing is helpful for documenting visual field loss, while an electroretinogram (ERG) will demonstrate severely decreased retinal amplitudes.

Differential Diagnosis

The differential diagnosis of retinitis punctata albescens includes other causes of flecked retina, including fundus albipunctatus, dominant (familial) drusen, fundus flavimaculatus, abetalipoproteinemia, oxalosis, cystinosis, talc emboli, Alport's syndrome, fleck retina of Kandori, and canthaxanthine retinopathy. Retinitis punctata albescens can be distinguished from fundus albipunctatus in that the ERG will be severely depressed and will not show improvement with dark adaption (as opposed to fundus albipunctatus which shows normalization in the rod response after a variable amount of dark adaption).

Prophylaxis

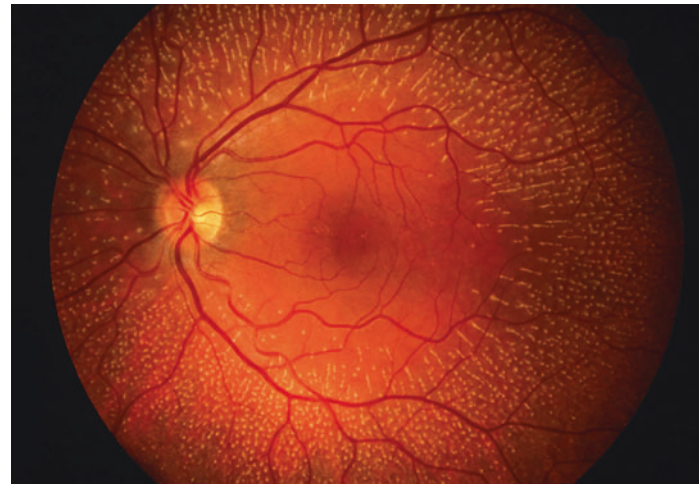
Although no prophylactic treatment is available for retinitis punctata albescens, routine screening of patients with a family history of retinitis pigmentosa allows early diagnosis and counseling.

Therapy

No cure exists for retinitis punctata albescens. Management involves treating associated causes of vision loss, including cataract and cystoid macular edema. Low vision aids and genetic counseling may also prove beneficial.

Prognosis

Retinitis punctata albescens behaves clinically like classic retinitis pigmentosa with the majority



Retinitis Punctata Albescens, Fig. 1 Color fundus photograph demonstrating typical fundus changes of retinitis punctata albescens, including numerous whitish-yellow flecks at the level of the retinal pigment epithelium (Photo courtesy of Dennis P. Han)

of patients experiencing progressive night blindness and loss of peripheral vision. Loss of central and color vision occur at more advanced stages of the disease.

Epidemiology

While the prevalence of retinitis pigmentosa as a group is estimated to be 1 in 5000, the prevalence of retinitis punctata albescens is not known. Retinitis punctata albescens tends to affect males and females equally and is most often inherited in an autosomal recessive pattern (Fig. 1).

Cross-References

- ▶ Alport Disease/Syndrome, Renal
- ▶ Atypical Retinitis Pigmentosa (RP)
- ▶ Dominant Familial Drusen
- ▶ Drusen
- ▶ Fundus Albipunctatus
- ▶ Fundus Flavimaculatus (Stargardt Disease/Juvenile Macular Degeneration)
- ▶ Retina, Structure of
- ▶ Retinal Pigment Epithelium
- ▶ Retinitis Pigmentosa, Decreased Vision in Neuro-Ophthalmology

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Retinoblastoma

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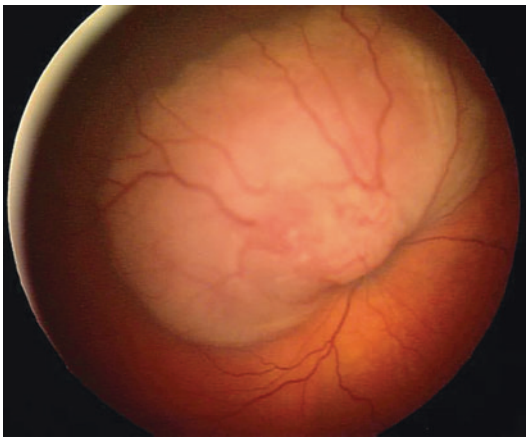
Definition

Retinoblastoma is a malignant neuroblastic tumor derived from the embryonic retinal cell.

Etiology

Retinoblastoma develops following mutations in both alleles of a cell's RB1 gene. The RB1 gene is

located on the long arm of chromosome 13 (13q14) and produces a nucleoprotein that regulates the transition of a cell from G1 to the S phase of the cell cycle. Loss of both RB1 alleles allows uncontrolled cellular proliferation. In approximately 40% of patients with retinoblastoma, loss of the first RB1 allele is inherited from either an affected parent (10%) or from a spontaneous mutation in one of the gametes (90%), and the loss of the second is spontaneous. In the remaining 60% of patients with retinoblastoma, loss of both RB1 alleles in the same cell is spontaneous (Murphree et al. 2006; Gass 1997; Shields 1999; Conway et al. 2005).



Retinoblastoma, Fig. 1 Color fundus photograph demonstrating a retinoblastoma tumors appear as yellow-white vascular masses of the retina with various growth patterns

Clinical Presentation

Retinoblastoma commonly presents as leukocoria (white pupil) or strabismus in a young child. Other less common signs include vitreous hemorrhage, hyphema, red eye, glaucoma, proptosis, and pseudohypopyon. Average age at diagnosis is 12 months for patients with hereditary retinoblastoma and 24 months for patients with non-hereditary retinoblastoma. Patients with hereditary retinoblastoma can develop multiple and bilateral tumors.

Diagnostics

Retinoblastoma is principally a clinical diagnosis made with fundus ophthalmoscopy using scleral depression during an exam under anesthesia. Retinoblastoma tumors appear as yellow-white vascular masses of the retina with various growth patterns (Fig. 1). Exophytic tumors grow into the subretinal space and induce an exudative retinal detachment. Endophytic tumors grow into the inner retina, where they can breakthrough into the vitreous and produce vitreous tumor seeds. Diffuse infiltrative tumors grow laterally within the retina and often display no discrete mass effect. Trilateral retinoblastoma involves concurrent growth of a tumor in the pineal gland.

Various ancillary tests are helpful for supporting a diagnosis of retinoblastoma. Ocular echography of the retinal tumor can suggest intralesional calcium by demonstrating tumor shadowing. Intralesional calcium is fairly specific for retinoblastoma. Computed tomography (CT) can also demonstrate the presence of intralesional calcium but does involve radiation exposure which can increase the risk of secondary cancers, especially in patients with hereditary retinoblastoma. Magnetic resonance imaging (MRI) of the orbit and head is valuable for excluding the presence of extraocular tumor extension and presence of a pineal tumor (trilateral retinoblastoma).

Histopathological diagnosis of retinoblastoma in enucleated eyes involves indentifying fleurettes and Flexner-Wintersteiner rosettes, both of which represent early degrees of retinal cellular differentiation.

Differential Diagnosis

The differential diagnosis of retinoblastoma includes persistent hyperplastic primary vitreous, Coat's disease, ocular toxocariasis, retinopathy of prematurity, cataract, chorioretinal colobomas, congenital retinal folds, retinal dysplasia, vitreous hemorrhage, uveitis, and other tumors (e.g., retinoma, astrocytic hamartoma, choroidal hemangioma, and diktyoma).

Prophylaxis

There is no true prophylaxis against retinoblastoma formation. Nonetheless, individuals carrying the RB1 mutation who are trying to have children can undergo preimplantation genetic testing with subsequent in vitro fertilization. Routine screenings with exams under anesthesia are recommended during the first several years of life for all babies with a family history of retinoblastoma.

Therapy

Treatment of retinoblastoma varies according to size and extent of tumor formation. Local therapy with transpupillary thermotherapy laser photocoagulation, cryotherapy, or plaque brachytherapy is appropriate for small tumors. Chemoreduction followed by local therapy may be necessary when a tumor is too large to be managed with local therapy alone. Often, one to six cycles of chemotherapy using a combination of vincristine, etoposide, and carboplatin can shrink a tumor enough so that local therapy is then appropriate. External beam radiation teletherapy, once a mainstay of treatment, is currently falling out of favor due to its association with secondary malignancies and craniofacial deformities in the field of radiation. Nonetheless, it can still be valuable for some advanced tumors. Primary enucleation remains standard of care for eyes with advanced retinoblastoma and no useful vision potential.

Treatment of extraocular retinoblastoma is complex and often involves a combination of systemic chemotherapy, external beam radiation teletherapy, and bone marrow transplantation. Gamma knife radiation therapy with intrathecal chemotherapy may be helpful for intracranial trilateral retinoblastoma.

Prognosis

Overall survival prognosis for patients with retinoblastoma confined to the eye is good with estimates greater than 90%. Poor prognostic indicators include tumor invasion of the optic nerve posterior to the lamina cribrosa, massive choroidal involvement, trilateral disease, and distant metastatic disease at the time of presentation. Individuals with heritable disease display a 1% chance per year during their lifetime of developing a secondary neoplasm.

Epidemiology

Retinoblastoma remains the most common malignant intraocular tumor of childhood with an estimated incidence of 1 in 15,000 live births (range 1:14,000–1:20,000). Most patients are diagnosed before 5 years of age. Males and females are equally affected and there is no predilection for any particular race.

Cross-References

- ▶ Astrocytoma
- ▶ Astrocytoma (Astrocytic Hamartoma)
- ▶ Coats' White Ring
- ▶ Cryptophthalmos
- ▶ Enucleation
- ▶ Helical Computed Tomography
- ▶ Metastatic Endophthalmitis
- ▶ Retina, Structure of
- ▶ Retinopathy of Prematurity

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Retinochoroidal Coloboma

► Ectasia, Retinal

Retinopathy

► Desferrioxamine Retinopathy

Retinopathy of Prematurity

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Definition

Retinopathy of prematurity (ROP) is a disease seen in premature infants having incomplete, vascularized retinas with a peripheral avascular zone. At gestational age earlier than 30 weeks, vascular endothelial growth factor (VEGF) and insulin-like growth factor I (IGF-I) influence abnormal growth of the retinal blood vessels as they develop from the optic disk toward the nasal ora serrata and finally reaching the temporal ora serrata.

Etiology

Smaller weight babies (1,250 g or less) and those with early gestational age (30 weeks or earlier) are at the highest risk for development of ROP.

Exposure to oxygen is a poorly understood risk factor. Currently, it is thought that the pathogenesis of ROP is biphasic. In the first phase seen at 22–30 weeks, the retina is hyperoxic. VEGF levels are low and the retinal blood vessels stop growing. The decrease blood vessel growth is thought to be due to low levels of IGF-I, low birth weight of less than 1,500 g as well as exposure to oxygen.

In the second phase seen around 32 weeks, neovascularization begins due to rising VEGF levels responding to the hypoxic avascular retina.

Clinical Presentation

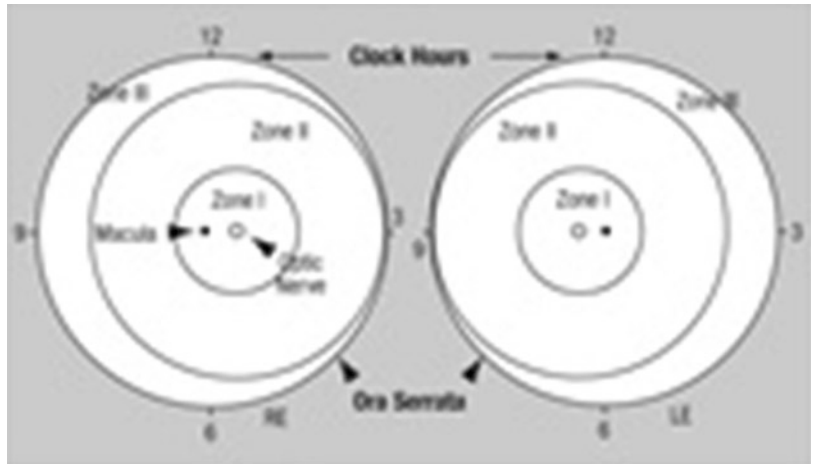
Not all premature babies who are premature develop ROP. About 90% of all infants with ROP are in the mild category and do not need treatment; only periodic ophthalmic observation. Weekly observation beginning at the fourth week of birth is to detect any disease progression to the more advanced stages of ROP and/or pre-plus disease as to prevent blinding eye disease.

ROP is classified in five stages, ranging from mild (stage I) to severe (stage V):

Stage 1 – mildly abnormal blood vessel growth that usually resolves without treatment. Children go on to develop normal vision and there is no further disease progression.
Stage II – moderately abnormal blood vessel growth that usually resolves without treatment. Children have normal vision and no further disease progression.
Stage III – severely abnormal blood vessel growth. Often plus disease develops requiring treatment
Stage IV – partially detached retina. Traction from the scar produces bleeding; abnormal vessels pull the retina
Stage V – completely detached retina and the end stage of the disease. If the baby is not treated, there is severe damage and even blindness.

Diagnostics

At 4–6 weeks of age, pupil dilation is performed using phenylephrine (1–2% combined with cyclopentolate (0.2–0.5%) or tropicamide (0.5–1%)). Using a lid speculum, the sclera is gently depressed while performing a thorough examination wearing binocular indirect ophthalmoscope. There is an international classification of ROP into anterior and posterior zones based on the optic nerve position. The degree of disease



Retinopathy of Prematurity, Fig. 1 International Classification of ROP

involvement is divided into 30° clock hours. Disease is staged depending on observation of the following problems. See Fig. 1.

Signs and symptoms include optic nerve pallor, enlarged cup in the optic nerve, retina detachment, dragged folds, attenuated or dilated or tortuous vessels, hemorrhage, neovascularization, pigment changes, and retrolental mass. In the vitreous, there may be haze or traction. There may be the appearance of myopia, strabismus, glaucoma, cataract, or anisometropia.

ETROP Classification of Disease (Early Treatment for Retinopathy of Prematurity)

Type 1 ROP – need prompt treatment within 48 h

Zone 1: any stage with plus disease
Zone 1: stage 3 without plus disease
Zone II: stage 2 or 3 with plus disease

Type 2 ROP – not severe enough to require treatment

Zone 1: stage 1 or 2 without plus disease
Zone II: stage 3 without plus disease

Stage 1 ROP signifies development of a demarcation line between the normal retinal vessels and avascular retina. The line has significant height and width and extends above the retina surface.

Stage 2 ROP signifies development of a demarcation ridge between the normal retinal vessels and avascular retina.

Stage 3 ROP signifies neovascularization in the stage 2 demarcation line and leads to extraretinal proliferation of tissue. The ridge may bleed and cause traction on the ridge. Due to retinal ischemia, vessels grow into the vitreous gel, causing fibrous proliferation, traction over the ridge, and eventually retinal detachment. At this point, the classification is considered type 1 ROP requiring immediate laser intervention to arrest disease progression.

Stage 4 ROP defines retinal detachment sparing the macula as 4A and involving the macula as 4B.

Stage 5 ROP signifies complete retinal detachment and necessitates an immediate and very difficult surgery to attempt to reattach the retina. Stage 5 has a very poor prognosis.

(Lab Diagnostics)

Prophylaxis

Timely detection of ROP depends on examination by a trained pediatric ophthalmologist beginning at week four.

Therapy

In type 1, laser photocoagulation treatment is currently and strongly recommended. 100–3,000 laser spots may be needed depending on the extent of zone involvement; whereas in type 2 it is preferable to observe and see if there progression to type 1, then treat. In the study (BEAT-ROP) bevacizumab versus laser treatment was tried but the disease recurred. The advantage of bevacizumab is that there appears to be a lower incidence of very high myopia (>8 diopters). Despite the trial outcome, presently, there is concern using anti-VEGF agents on the developing vasculature of premature infants. In later stages of ROP, other treatment options include a scleral buckle and vitrectomy. In post-laser treatment, lubricant and anti-inflammatory eye drops are prescribed.

Prognosis

Myopia can develop in both treated and untreated infants. With high myopia, strabismus can occur.

Epidemiology

The incidence of ROP is rising, given the fact there are many more surviving premature infants. Also, babies requiring treatment is lower among African American than non-African American babies.

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Retinoschisis

▶ Degenerative Retinoschisis, Typical and Reticular

Retractors, Lower Eyelid

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Synonyms

Capsulopalpebral fascia; Inferior tarsal muscle; Müller's muscle

Definition

The lower eyelid retractors consist of the capsulopalpebral fascia and the inferior tarsal muscle. The inferior tarsal muscle is occasionally referred to as Müller's muscle of the lower eyelid.

Structure

The capsulopalpebral fascia arises proximally as the capsulopalpebral head, which comprises fascial extensions from the terminal muscle fibers and tendon of the inferior rectus muscle (Hawes and Dortzbach 1982). The fibroelastic capsulopalpebral head then splits into two and straddles the inferior oblique muscle before reuniting as Lockwood's ligament. The tissue anterior to Lockwood's ligament has traditionally been termed the capsulopalpebral fascia. The majority of the capsulopalpebral fascia extends anterosuperiorly to insert on the inferior tarsus, inferior fornix, and Tenon's capsule on the surface of the globe, while the inferior portion extends through the orbital fat to the orbital septum.

The lower eyelid retractor has often been thought of as a single layer that incorporates the smooth muscle fibers of the inferior tarsal muscle, which are most prevalent near the inferior fornix (Hawes and Dortzbach 1982). More recently, however, the lower eyelid retractor has been described to be in a double-layer configuration (Kakizaki et al. 2006; Kakizaki et al. 2009). The double-layer configuration is also present in Asian eyelids, where there is often a higher or more indistinct line of fusion of the orbital septum to the capsulopalpebral fascia (Kakizaki et al. 2009). The posterior layer of the retractor consists of a dense fascial layer that includes the smooth muscles that comprise the inferior tarsal muscle, while the anterior layer extends from Lockwood's ligament and merges with the orbital septum and suborbicularis fascial layer, before extending through the orbicularis oculi to the anterior lamellae of the lower eyelid. The ability to separate the anterior and posterior lower eyelid retractor layers may have clinical implications in the treatment of eyelid malposition, especially as the posterior layer has been reported to be responsible for the main tractional forces on the lower eyelid.

The lower eyelid retractor functions in tandem with the inferior rectus, which is in turn innervated by the inferior division of the oculomotor nerve. The smooth muscles of the inferior tarsal muscle are sympathetically innervated, analogous to the Müller's muscle of the upper eyelid.

Function

The lower eyelid retractors effectuate inferior movement of the lower eyelid, as well as widening of the interpalpebral fissure in conjunction with the upper eyelid retractors. The lower eyelid retractors exert rotational forces on the tarsus and play a role in normal and abnormal eyelid margin positioning.

Clinical Relevance

The lower eyelid retractors are intrinsically involved in disorders of lower eyelid position as they contribute to the vertical stability of the eyelid. Lower eyelid retractor atrophy, loosening, or dehiscence results in decreased vertical stability of the eyelid, allowing eyelid margin rotation resulting in entropion or ectropion. Lower eyelid retractor dehiscence or disinsertion may be reversed with surgical advancement and reattachment of the retractors to the inferior tarsus (Tse et al. 1991). The Jones entropion procedure is a commonly performed method of involutional entropion repair where the anterior surface of the lower eyelid retractor is identified without separating the posterior aspect of the retractor from the conjunctiva. Isolated advancement of the posterior layer of the lower eyelid retractor has also been reported to be effective in entropion repair.

In lower eyelid retraction, there is often a relative or absolute shortening of the posterior lamella and eyelid retractors. Common causes of lower eyelid retraction include thyroid ophthalmopathy, chemical burns, cicatrizing conjunctival diseases, and trauma. Lower eyelid retraction is frequently managed by recession of the lower eyelid retractors and interposition of a spacer graft to provide increased length. Autologous tissue grafts such as hard palate mucosa have been reported to be effective donor tissue (Kersten et al. 1990).

Knowledge of the anatomy of the lower eyelid retractors is also important in strabismus surgery that involves the inferior rectus. Manipulation of the inferior rectus concurrently alters the lower eyelid retractor complex, resulting in increased lower eyelid retraction after inferior rectus recessions and vice versa. Careful dissection of the fascial and connective tissues surrounding the inferior rectus is important to minimize undesired eyelid positional changes after strabismus surgery.

As a consequence of the sympathetic innervation of the smooth muscles of the inferior tarsal muscle, medical conditions that potentiate sympathetic innervation such as thyroid dysfunction can lead to increased eyelid retraction and inferior scleral show. Increased exposure of the ocular surface and cornea may lead to secondary dry eyes or keratopathy.

Cross-References

▶ Congenital Entropion

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Retrobulbar Block

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Definition

Retrobulbar block is a regional anesthetic nerve block used in intraocular procedures. In retrobulbar injection, local anesthetic is injected behind the eye, into the muscle cone of the extraocular muscle, which is located inside the orbital space, the area located behind the globe of the eye. Injection of local anesthesia provides akinesia of the extraocular muscles by blocking cranial nerves II, III, and VI, which prevents movement of the globe. Retrobulbar block also provides sensory anesthesia of the cornea, uvea, and conjunctiva by blocking the ciliary nerves.

Usual retrobulbar block includes either 1–2% lidocaine (Xylocaine) and 0.5–0.75% bupivacaine (Marcaine). Lidocaine enables quick anesthesia but has shorter duration, whereas bupivacaine has a longer duration but also takes longer time to achieve anesthesia. A mixture of both compounds is ideal to achieve quick and long-lasting (up to 2–3 h) anesthesia. The volume of liquid injected is between 4 and 6 cc, and up to 8 cc is considered safe. It is important to avoid bupivacaine mixture with epinephrine, because epinephrine may cause vasoconstriction and may cause central retinal artery occlusion. In the past, hyaluronidase – an enzyme – was frequently used as an adjuvant to the anesthetic solution, as it accelerates and improves dispersal of the agent, but in recent years, the enzyme is rarely used and hard to find. The injection is performed using a needle (22–27 Gauge, 3 cm long) – either special retrobulbar needle with blunt-end or regular hypodermic needle. By using a blunt-end needle, there is less likelihood of causing globe perforation, but insertion of the blunt needle is more painful as compared to sharp-end needle. The needle is inserted at the 1/3 inferolateral border of the bony orbit and directed straight back until it has passed the equator of the globe. It is then directed medially and upward toward the apex of the orbit. Occasionally a "pop" is felt as the needle tip passes through the muscle cone delineating the retrobulbar space. Following a needle insertion, gentle aspiration is performed to ensure that the needle is not situated inside an artery or vein, and then anesthesia solution is slowly injected. Proptosis of the globe is usually the first sign that the injection is in its proper position.

This block was previously employed abundantly for cataract surgery, but in recent years, its use has decline due to the widespread use of topical anesthesia and currently is used predominantly in complicated vitreoretinal procedures.

Retrobulbar block is associated with serious vision and life-threatening complications. Ocular adverse events include hematoma formation, optic nerve damage, and perforation of the globe with possible blindness. Systemic complications include local anesthetic toxicity, brainstem anesthesia, and stimulation of the oculocardiac reflex.

Cross-References

▶ Anatomic Reattachment Surgery, for Retinal Detachment

▶ Anterior Segment Surgery
▶ Cataract Surgery
▶ Topical Anesthesia in Eye Surgery

Retrobulbar Hemorrhage

▶ Orbital Hemorrhages

Retrobulbar Hemorrhage, Optic Nerve Dysfunction

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Definition

Retrobulbar hemorrhage is an uncommon, vision-threatening complication of the orbit that in some instances can lead to irreversible loss of vision. The loss of vision can be attributed to the development of orbital compartment syndrome with secondary ischemia, increased intraocular pressure, or direct compression of the optic nerve.

Epidemiology

One study reported 115 cases of nontraumatic orbital hemorrhage over a 24-year period (Sullivan and Wright 2000). Retrobulbar hemorrhage can affect any age, either gender, and any race depending on underlying etiology although trauma and surgery are common causes.

Clinical Features

The most common symptoms and signs of retrobulbar hemorrhage include ipsilateral orbital pain, pressure, ophthalmoplegia, proptosis, and loss of vision. Patients may complain of headache, diplopia, nausea, and vomiting (Lewis and Perry 2007). Signs of an acute retrobulbar hemorrhage are usually obvious and include a tense orbit, rapidly progressive proptosis, ophthalmoplegia, increased intraocular pressure, visual loss, and a relative afferent pupillary defect. Funduscopy might show a normal or swollen optic disk and retinal vascular occlusive disease (Lewis and Perry 2007).

Tests

Due to the emergent nature of the sight-threatening acute retrobulbar hemorrhage, a surgical decompressive treatment (e.g., lateral canthotomy and cantholysis) is often initiated before the orbital imaging studies to confirm the diagnosis (Goodall et al. 1999).

Typically orbital computed tomography (CT) scans are preferred because of their faster acquisition time and better visualization of the bony anatomy and the retrobulbar hemorrhage (Lewis and Perry 2007).

Differential Diagnosis

(a) Diplopia
(b) Proptosis
(c) Hyperthyroid
(d) Cavernous sinus thrombosis

Etiology

Retrobulbar hemorrhage has many different etiologies. Some of these etiologies include trauma, retrobulbar anesthetic injection, and periocular surgery or may rarely occur spontaneously (Lewis and Perry 2007).

Diagnosis

The diagnosis is primarily made by the typical clinical signs and symptoms of the retrobulbar hemorrhage. In some cases, however, it may be necessary to utilize an orbital CT to confirm the diagnosis.

Treatment

The treatment regimen will depend on the urgency of the situation. Although oxygen therapy, intravenous (IV) mannitol, oral or IV acetazolamide, steroids, and topical beta-blockers (Wolfort et al. 1999) have been used, the mainstay of acute treatment is surgical decompression.

The preferred methods to decrease the elevated orbital and intraocular pressure are urgent lateral canthotomy and cantholysis (Goodall et al. 1999).

Cross-References

- ▶ Binocular Diplopia
- ▶ Optic Disc (Optic Nerve Head)
- ▶ Optic Neuropathy
- ▶ Relative Afferent Pupillary Defect (RAPD)

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Retrobulbar Optic Neuritis

▶ Optic Neuritis: Overview

Retrobulbar Optic Neuropathy

▶ Posterior Ischemic Optic Neuropathy

Retrochiasmal Disorders

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Synonyms

Lateral geniculate lesion; Occipital lobe lesion; Optic tract lesion; Parietal radiations lesion; Temporal radiations lesion

Definition

The retrochiasmal pathway begins posterior to the optic chiasm with the optic tracts then travels to the lateral geniculate nuclei, the temporal lobe optic radiations (i.e., Meyer's loop), the parietal lobe optic radiations, and ends in the occipital cortex. At the optic chiasm, fibers from the nasal retina cross over to the contralateral side, while temporal fibers remain on the ipsilateral side creating visual field defects that are on the same side (i.e., homonymous) and respect the vertical meridian (hemianopic). As the optic fibers course posteriorly along the visual pathway, they become more organized so that fibers from a similar origination of the retina run in closer and closer proximity to one another. In general, the further posterior the lesion (e.g., occipital) along the retrochiasmatic pathway the more congruous (the same size, shape, and density on each side) is the homonymous hemianopic defect. Thus, occipital lobe lesions demonstrate the most congruity and optic tract lesions the least congruity. Unfortunately, the specificity of congruity for occipital lobe lesions is not 100% and highly congruous visual field defects can also occur in more anterior retrochiasmal lesions.

Etiology

1. Ischemic
2. Hemorrhagic
3. Traumatic
4. Neoplastic
5. Demyelinating
6. Infectious
7. Inflammatory
8. Degenerative

Clinical Presentation

Retrochiasmal lesions typically present with a contralateral HH. The patients typically complain of a problem with their "side vision," but the complaint may be more vague (e.g., "blurry vision", "difficulty reading") and some patients only notice the temporal visual field loss in their HH. For a right HH, there is often difficulty finding the next word during reading and for left homonymous hemianopsia there may be more difficulty finding the next line while returning to the left side of the text. The patient or their spouses or family may complain that the patient hits the curb or garage or has hit the side-mirror on the side with temporal visual field loss. Some patients, especially if in long-standing or in cases of degenerative disease, do not realize that they have a visual field defect and it may be found incidentally on routine eye exam.

In retrochiasmal lesions, patients will not complain of decreased visual acuity (regardless of macula sparing or splitting HH) unless they have another visual pathway lesion (e.g., cataract, retinopathy, or optic neuropathy) affecting the central vision or the retrochiasmal lesion is bilateral (i.e.,. juxtaposed bilateral HH). In addition, depending on the underlying etiology (e.g., cerebral tumor, brain hemorrhage or edema, AVM, etc.), the patient might have headache or other focal neurologic symptoms or signs in association with their HH. Occipital cortex lesions typically have no other signs or symptoms however.

- Occipital lobe lesions: Typically occipital lesions produce HH in isolation. Lesions of the occipital lobe can, however, produce unformed visual hallucinations, such as blotches of color or light. These hallucinations typically appear in a constant homonymous hemianopic distribution and do not alternate sides (which helps to distinguish them from migraine with aura). Association cortex involvement, however, might produce visual processing defects and agnosias.
- Temporal lobe lesions: May be characterized by cortical deafness; loss of ability to comprehend music or language; Wernicke type aphasia; memory loss; complex, multimodal hallucinations; or seizures (i.e., temporal lobe epilepsy).
- Parietal lesions: A patient with a lesion to the nondominant parietal lobe may experience

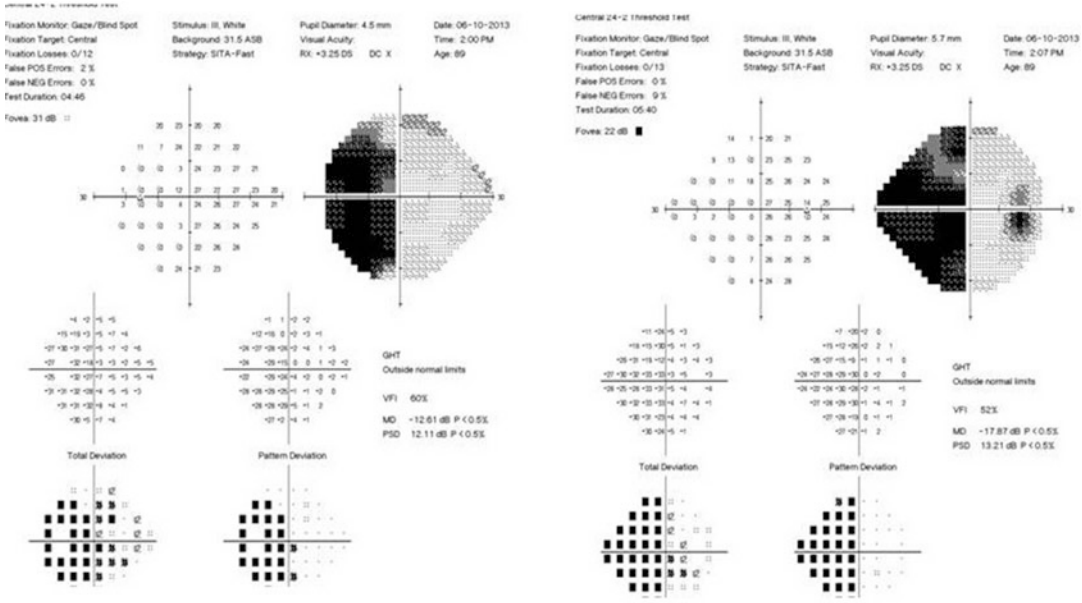
contralateral neglect and constructional apraxia. Damage to the dominant parietal lobe can result in Gerstmann Syndrome, which includes right-left confusion, difficulty with writing (agraphia), difficulty with mathematics (acalculia), and disorders of language (aphasia). In addition, the ipsilateral parietal lobe provides supranuclear control of smooth pursuit and thus in a patient with a complete HH there might be asymmetric impairment of the optokinetic nystagmus (OKN) response, indicating a parietal localization over occipital lobe lesions which would be expected to have a symmetric OKN response.

Diagnostic

1. The optic tract carries the visual fibers from the chiasm to the lateral geniculate body but also the afferent pupil fibers to the midbrain. Thus patients with an optic tract lesion might also have a relative afferent pupillary defect and band type optic atrophy in the eye with the temporal visual field loss (i.e., nasal fiber loss). The HH tends to be incongruous in optic tract lesions.
2. The lateral geniculate body (LGB) is a highly organized structure where the retinal fibers in the optic tract synapse. LGB lesions are rare but may produce characteristic and localizing visual field defects due to the unique blood supply of the LGB. Both the lateral choroidal artery (a branch of the posterior cerebral artery) and the anterior choroidal artery (a branch of the internal carotid artery) supply the LGB. With lateral choroidal artery disruption, the patient will have a contralateral homonymous hemianopsia in a wedge-shaped distribution, with sparing of the most superior and inferior aspects of that field. In contrast, with anterior choroidal disruption, the patient will have a contralateral homonymous hemianopsia with loss of the upper and lower quadrants that spares a symmetrical inner wedge, termed a quadruple sectoranopia.
3. Damage to the temporal lobe radiations (Meyer's loop) gives a contralateral homonymous hemianopsia that is denser superiorly (i.e., "pie in the sky quadrantanopia") because these radiations include the more inferior retinal fibers (which correspond to the superior aspect of the visual field). These HH may be incongruous suggesting a more anterior localization in the retrochiasmal pathway. The optic tract lesion can be distinguished sometimes from temporal lobe by the presence of an RAPD and band type optic atrophy in the optic tract lesion.
4. The parietal lobe radiations typically produce an incongruous homonymous hemianopsia that is denser inferiorly (from superior fiber involvement).
5. Occipital lobe lesion – depending upon whether the inferior or superior calcarine cortex is involved, the homonymous hemianopsia can be denser superiorly or inferiorly (see Fig. 1). The HH in occipital lesions tends to be congruous and macular sparing. There might also be selective involvement or sparing of the monocular temporal crescent. This temporal crescent (60–90° temporally) of contralateral visual field (crossed nasal fibers) has no correlate in the nasal field of the fellow eye and is represented monocularly in the anterior portion of the calcarine cortex.

Differential Diagnosis

Patients with unexplained HH should undergo a full neurologic exam looking for localizing features. A careful pupil and fundus exam in addition to formal visual field testing should be performed to look for an RAPD or band atrophy in an optic tract lesion and to define localizing features of the HH including laterality, congruity, macular sparing or splitting, and the presence or absence of the monocular temporal crescent. Neuroimaging (preferably MRI with and without contrast of the head) is recommended for unexplained HH. In the acute setting, a non-contrast CT scan might be superior to look for acute blood or to expedite the evaluation and treatment of the underlying etiology (especially for acute stroke).



Retrochiasmal Disorders, Fig. 1 Retrochiasmal lesion with left homonymous hemianopsia

Prophylaxis

Not applicable

Therapy

Treatment depends upon the etiology of the lesion.

Prognosis

Prognosis depends upon the etiology of the lesion.

Epidemiology

The retrochiasmal lesion can occur in any age, any race, and either gender. In most pooled large aggregate studies, the most common etiology of a HH in adults is ischemic or hemorrhagic stroke but any structural lesion of the retrochiasmal pathway may produce a HH. Older vasculopathic patients presenting with an acute HH should be evaluated for stroke or hemorrhage. Patients with optic tract lesions often have a compressive lesion.

Cross-References

- ▶ Demyelinating Disease
- ▶ Mild Traumatic Brain Injury (MTBI)
- ▶ Papilloma
- ▶ Relative Afferent Pupillary Defect (RAPD)

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Retro-Orbicularis Oculi Fat (ROOF)

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Synonyms

Brow fat pad, superior extension of the sub-brow fat pad; Submuscular fibroadipose tissue; Suborbicularis fibroadipose tissue

Definition

Retro-orbicularis oculi fat (ROOF) is a superficial fat layer existing between the orbicularis oculi muscle and the periosteum of the supraorbital bone, superior to the orbital septum.

Structure

ROOF is a superior extension of the sub-brow fat pad and is a layer of fibroadipose tissue that is situated deep to the orbicularis oculi and superficial to the periosteum of the supraorbital bone. It extends medially beyond the midsupraorbital rim and laterally beyond the lateral orbital rim (Zide 2006). The superior portion of ROOF extends upward under the frontalis muscle and contributes to the galeal fat pad over the superolateral orbital rim (Prendergast 2013). Although ROOF consists of the same tissue as the sub-brow fat pad, it is thicker than the sub-brow fat pad and can contribute to the bagginess and bulky hood of the lateral upper eyelid in some patients (Kakizaki et al. 2009).

Function

ROOF contributes to the fullness (in youth) and heaviness (in senescence) of the lateral brow and lid.

Clinical Relevance

With age, deflation of the ROOF contributes to the hooding that occurs in the eyebrow and upper eyelid region. Endoscopic brow lift, which may include reinflation via fat transfer in the ROOF plane, can restore the more youthful three-dimensional contour of the eyebrow (Hoenig 2010).

ROOF resection alone is often efficacious in improving the thickness and heaviness of the upper eyelid in Caucasians (Kakizaki et al. 2009). However, because Asians often have a more substantial sub-brow fat pad, it is often necessary to additionally resect the sub-brow fat pad in Asians to produce an aesthetic "double eyelid" (Kakizaki et al. 2009; Tan et al. 2011).

A large venous channel often passes from the area of the supraorbital region laterally to the ROOF region. This vessel may lead to bleeding and should be anticipated during surgery (Zide 2006).

ROOF's corresponding adipose tissue in the lower eyelid is called the "suborbicularis oculi fat" (SOOF).

Cross-References

▶ Sub-brow Fat Pads

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Rhabdomyosarcoma of Orbit

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Definition

Orbital rhabdomyosarcoma (RMS) is the most common primary orbital malignancy of childhood and accounts for 8% of all cases of primary RMS. The tumor arises from undifferentiated mesenchymal cells and most commonly presents with rapidly progressive, unilateral proptosis and globe displacement. With greater than 90% cure rate if discovered prior to orbital invasion, prompt recognition and treatment are essential.

Etiology

The majority of cases of RMS are sporadic. Reported risk factors include germline p53 mutations, ionizing radiation, associated central nervous system anomalies, maternal/paternal use of marijuana and cocaine, and first-trimester prenatal X-ray exposure. Additionally, familial cancer syndromes (e.g., Li-Fraumeni) have been associated with RMS.

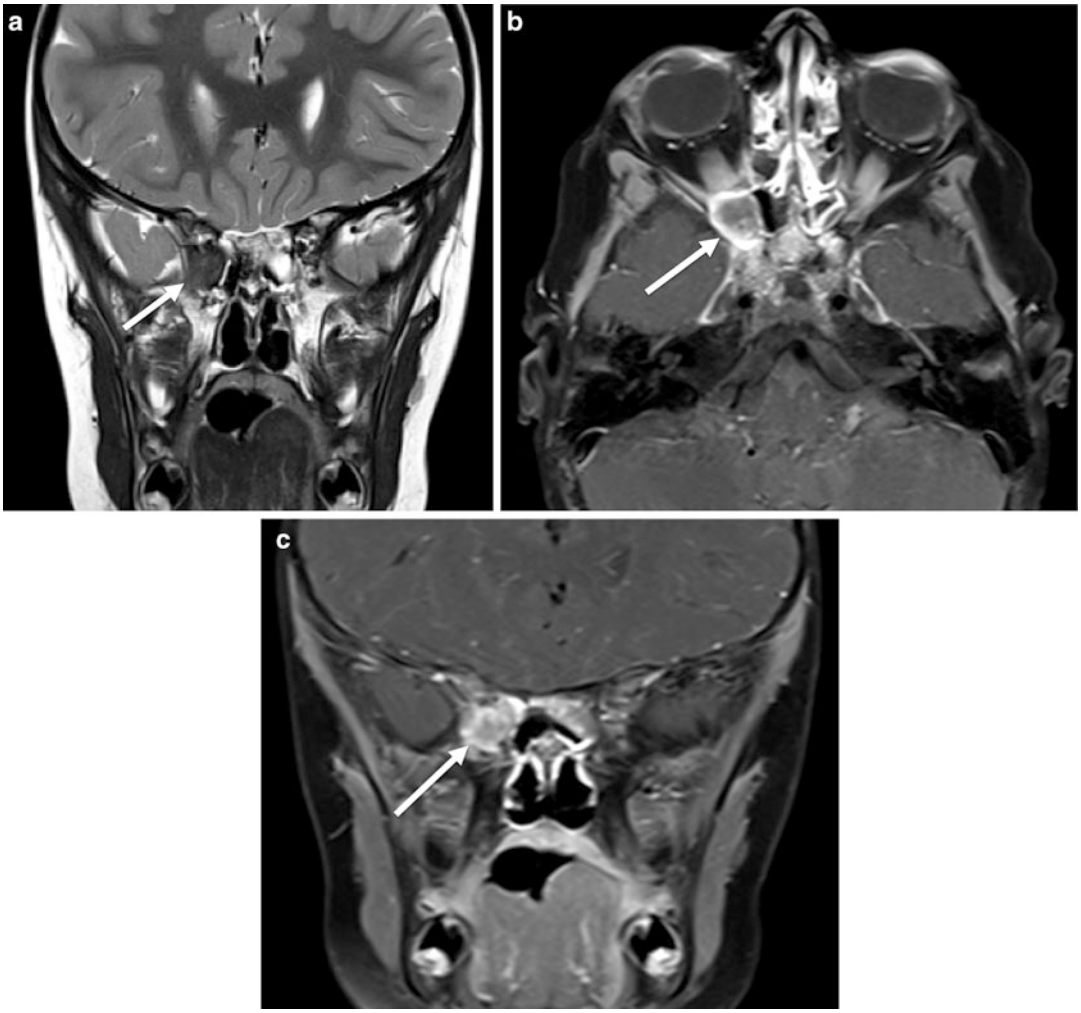
RMS is currently classified based on histologic subtype, with the embryonal subtype (ERMS) representing the most common variant (70–80% of cases). ERMS most often occurs in the head, neck, and genitourinary tract of young patients. Loss of heterozygosity at the 11p15.5 locus with resulting dysfunction of tumor suppressor genes has been implicated in the etiology of ERMS. Alveolar RMS (ARMS) is the second most common histopathologic subtype identified. A characteristic translocation of FKHR(FOX01A) gene at chromosome 13 with PAX3 or PAX7 results in tumorigenic behavior. The botryoid variant, a rare subtype of ERMS, invades the orbit secondarily by extension from the paranasal sinus or conjunctiva. Grossly, the botryoid variant appears grapelike.

Clinical Presentation

Classic presentation for RMS is rapidly progressive, unilateral proptosis. In older patients, proptosis can be more gradual, occurring over weeks to months. With superior orbital tumors, the globe is typically displaced downward, often with associated blepharoptosis, diplopia, or extraocular motility dysfunction. In 25% of cases, a firm mass is palpable; however, tumors may present in the retrobulbar space or conjunctiva. ARMS has propensity for the inferior orbit. With an anterior orbital location, significant soft tissue edema, eyelid dislocation, or chemosis may occur. Large tumors can cause choroidal folds or disc edema/optic neuropathy. Pain is reported in 10% of cases on presentation. History of unrelated trauma may confuse the clinical picture and can lead to delay in diagnosis and treatment.

Diagnostics

When concern for RMS arises, workup should proceed urgently. Both CT and MRI can be used to identify the lesion and determine the preliminary extent of invasion. Appearance on CT is of an extraconal mass that is isodense to muscle. The majority of tumors (2/3) are located in the superonasal quadrant, and half extend into the intraconal space. Bony destruction is found with large and/or aggressive lesions. More commonly, the tumor conforms to the bony walls of the orbit or the globe. Enhancement is always present and may be uniform or heterogeneous if there is necrosis or hemorrhage within the mass. Internal hemorrhage may produce focal areas of increased signal on both T1- and T2-weighted images and focal areas of hyperdensity on CT scan. MRI is useful to identify invasion of the surrounding soft tissues or intracranial extension (Fig. 1).



Rhabdomyosarcoma of Orbit, Fig. 1 (**a**) T2-weighted coronal image of an embryonal rhabdomyosarcoma in a young child demonstrates a focal T2 hypointense mass (*arrow*) at the orbital apex extending to the superior orbital fissure. (**b**) Fat-saturated T1-weighted post-gadolinium (**b**) axial and (**c**) coronal images demonstrate heterogeneous enhancement within this lesion (*arrows*)

When a pseudocapsule is present, prompt excisional biopsy should be undertaken, usually via an anterior orbital approach. Fine needle aspiration will be insufficient to provide tissue needed for frozen section, permanent light microscopy, electron microscopy, and immunohistochemistry. If the entire tumor cannot be reasonably removed due to location near vital structures or extent of invasion, as much tumor should be excised as is safe. There is suggestion that minimizing residual tumor burden will optimize subsequent radiation and chemotherapy and limit future treatment burden.

By histology, ERMS is composed of loose fascicles of undifferentiated small round or spindle-shaped cells. ARMS tumor cells are arranged in fibrovascular strands or nests, similar in appearance to lung alveoli. Electron microscopy may be necessary to identify cross-striations. Immunohistochemical markers of rhabdomyosarcoma include desmin, myoglobin, myogenin, MyoD1, vimentin, caveolin-3, and

muscle-specific actins. Cytogenetics helps differentiate and classify the primary orbital tumor type.

Referral to pediatric oncology is appropriate upon first suspicion of malignancy as concomitant diagnostic procedures may be necessary at the time of orbital biopsy. Any palpable nodes require biopsy to rule out regional metastasis. Lab testing including complete blood count, comprehensive metabolic panel, liver function testing, and urinalysis should be obtained. Rarely, tumor-induced disseminated intravascular coagulation (DIC) may be present, and coagulation profile is therefore necessary. Metastatic workup may further include CT chest, bone scan, bone marrow sampling, and PET scan. Metastatic spread occurs hematogenously, most commonly to the lung and bone.

Differential Diagnosis

Orbital RMS should be on the differential for any child presenting with progressive proptosis. Additional clinical findings of globe displacement, eyelid edema, and conjunctival congestion stimulate a broad differential in the pediatric population. Inflammatory (idiopathic orbital inflammation, allergy), infectious (orbital cellulitis, conjunctivitis, dacryocystitis), or neoplastic (capillary hemangioma, Langerhans cell histiocytosis, lymphangioma) alternatives must be considered.

Therapy

Treatment involves multimodal therapy including surgical excision followed by chemotherapy and/or radiation. All patients receive chemotherapy, the regimen dependent on Intergroup Rhabdomyosarcoma Study Group (IRSG) system and histologic subtype. The IRSG system is largely determined by the degree of residual tumor following surgical excision. Radiotherapy is performed on all cases except IRSG group I patients (those with completely resected localized lesions) with embryonal subtype.

Prognosis

IRSG staging and prognosis depend on primary site, histologic type, tumor size, degree of regional spread, nodal involvement, distant metastatic disease, and residual tumor following pre-chemotherapy surgical excision. Of all RMS types, an orbital primary location portends the best prognosis with an overall survival of over 90%. Children older than 1 and less than 10 years of age carry a more favorable prognosis. Alveolar tumors and distant metastases present at diagnosis are associated with worse prognosis.

Epidemiology

RMS represents 3% of all childhood cancers and is the third most common solid extracranial tumor behind neuroblastoma and Wilms' tumor. The incidence is reported to be 4–5 per million in children less than 15 years of age, and there is a slight male predominance (male/female ratio 1.4:1). Average age of onset is 6 years of age and there are two age peaks between 2–6 and 15–19 years. The 15–19 age peak presentation is more common in males. This malignancy can also develop in adults.

Cross-References

► Sarcoma, Orbital

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Rhombic Transposition Flap

► Transposition Flaps, for Lateral Canthal Defects

Riley-Day Syndrome (Familial Dysautonomia)

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Synonyms

Hereditary sensory and autonomic neuropathy (HSAN) III

Definition

A hereditary sensory autonomic neuropathy primarily affecting the sympathetic nervous system.

Etiology

Familial dysautonomia is an autosomal recessive disorder found predominantly in the Ashkenazi Jewish population. It is due to a mutation in the IkB kinase-associated protein (IKBKAP) gene which codes for the IKAP/hELP1 protein on the 9q31-q33 locus. This leads to the downregulation of genes involved in the expression of neurotransmitters critical for the development, differentiation, and survival of unmyelinated and small myelinated peripheral sensory and autonomic neurons. The sympathetic afferent and efferent pathways are both involved leading to impaired transmission of baroreceptor, visceral, and chemoreceptor information. There may also be a reduced number of parasympathetic ganglion cell complexes.

Clinical Presentation

Signs and symptoms of familial dysautonomia appear early in life and are generally identified in the pediatric population. They are related to loss of small sensory and autonomic fibers as well as supersensitivity to cholinergic and adrenergic agents. These include:

- Decreased pain and temperature
- Preservation of proprioception and touch
- Hemodynamic instability and dysautonomic crises:
  - Physiologic or psychologic stress leading to inappropriate cardiovascular response
  - Insensitivity to hypoxemia and hypercarbia leading to pulmonary insufficiency
- Hyporeflexia
- Corneal hypoesthesia:
  - Alacrima
  - Neurotrophic ulcers
- Poor oropharyngeal coordination (feeding difficulty, aspiration, reflux)
- Absence of fungiform papillae
- Erythematous skin blotching and hyperhidrosis
- Developmental delay but normal intelligence
- Ataxia
- Scoliosis

Diagnosis

Familial dysautonomia is largely a clinical diagnosis of the pediatric population.

Genetic testing is available at selected centers in the USA and Israel.

Clinical testing:

EMG (nerve function)
EEG (evaluation of seizures)
EKG (prolonged QT intervals and cardiac conduction)
Chest radiographs (atelectasis and pulmonary changes)

Urinary vanillylmandelic acid levels (decreased)
Homovanillic acid levels (increased)
Plasma dopamine β-hydroxylase (decreased)
Sural nerve biopsy

Differential Diagnosis

Hereditary sensory autonomic neuropathy, types I, II, IV, and V.

Prophylaxis

- Avoid medications that interact with the autonomic nervous system.
- Anxiolytic medications.
- Perioperative risk assessment and preparation.

Therapy

Treatment of familial dysautonomia consists of preventative and supportive care. These include maintaining eye moisture to prevent keratopathy, feeding strategies, and administration of agents to prevent dysautonomic crises (anxiolytics such as benzodiazepines, clonidine, etc.) and cardiovascular instability (fluid, plasma, blood products, and mineralocorticoids).

Prognosis

Dysautonomic crises begin around age 3 with attacks of cyclical vomiting, hypertension, sweating, and agitation. Fifty to 60% of children die before the age of 20 but there are reports of patients surviving until their 40s. The cause of death is usually related to aspiration, pulmonary failure, or cardiovascular instability.

Epidemiology

Occurs almost exclusively in the Ashkenazi Jewish population:

Riley-Day Syndrome (Familial Dysautonomia), Fig. 1 Riley-Day patient with neurotrophic keratopathy (Courtesy of Dr. Roger Langston)

- Incidence, 1–10,000 to 1–20,000
- Carrier frequency, 1:27–1:32

Clinical Photograph

See Fig. 1

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Rineton

► Intravitreal Triamcinolone

Ring Sign, in Idiopathic Orbital Inflammation

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Definition

The radiographic finding shows scleral uveal rim thickening with contrast enhancement and edema extending into Tenon's space producing the "ring sign" in nonspecific orbital inflammation.`

Etiology

In idiopathic orbital inflammation, an inflammatory infiltrate can affect the posterior portion of the globe and the retrobulbar fat pad. Scleral uveal thickening and enhancement may be caused by tenonitis with fluid in Tenon's space, producing a lucent area or "ring sign" on computed tomography (CT). On B-scan ultrasonography, an acoustically hollow area corresponding to an edematous Tenon's capsule can be seen.

Occurrence

Idiopathic orbital inflammation or orbital pseudotumor is a benign inflammatory syndrome of the orbit, although extra-orbital involvement can occur. It can cause symptoms of periorbital edema, erythema, proptosis, ptosis, diplopia, and pain with eye movements. Imaging with ultrasonographic (CT) and radiologic (MRI) examination plays an important role in the diagnosis of nonspecific orbital inflammation. Patients typically respond dramatically to high-dose corticosteroid therapy.

Classification

Orbital pseudotumor can be subclassified on the basis of the anatomic target areas within the orbit. It may be a diffuse process or more localized affecting the extraocular muscles (myositis), the lacrimal gland (dacryoadenitis), or the sclera and posterior tenons (scleritis). It is important to differentiate orbital pseudotumor from infection, neoplasm, and other causes of orbital inflammation including thyroid-associated orbitopathy, Wegener's granulomatosis, and lymphoproliferative disorders.

Cross-References

▶ Inflammatory Eye Disease
▶ Spiral Computed Tomography, in Orbital Evaluation

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Rod Monochromacy

▶ Achromatopsia (Rod Monochromatism), Gene Defects Causing

Rod-Cone Dystrophy

▶ Retinitis Pigmentosa, Decreased Vision in Neuro-Ophthalmology

Rosacea: Overview

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Synonyms

Acne rosacea

Definition

Ocular rosacea is ocular and eyelid inflammation due to rosacea, a chronic inflammatory condition that affects the skin on the face, nose, and forehead.

Etiology

The exact pathophysiology of rosacea is unknown, though it seems to be comprised of both innate and environmental factors. Recent research has shown an upregulation of proinflammatory and vasoregulatory genes in these patients (e.g., cathelicidin, kallikrein-5, and toll-like receptor 2). Various microbial organisms including *Helicobacter pylori*, *Demodex folliculorum*, *Demodex brevis*, and *Staphylococcus epidermidis* have also been implicated in the disease.

Clinical Presentation

Patients with ocular rosacea may complain of nonspecific symptoms, such as foreign body sensation, dryness, itching, photophobia, and tearing. Symptoms are usually bilateral. Ocular rosacea symptoms are usually not related to the severity of the cutaneous form of rosacea. In fact, in 20% of ocular rosacea patients, symptoms may occur before any cutaneous manifestations. Patients' eyelids, corneas, and conjunctiva can be affected depending on the severity of the condition.

Patients with ocular rosacea have also been found to have recurrent hordeolum and chalazion secondary to meibomian gland dysfunction which is common in this condition. Slit-lamp examination of the eyelid margins can reveal telangiectases, dilated meibomian glands, excessive seborrheic secretion, and collarettes around the eyelashes. There may be a soapy aspect of the inferior tear meniscus and debris in the tear film. Dry eyes, with abnormal Schirmer's test, and diminished tear breakup time (TBUT) were reported in a large majority of patients with ocular rosacea. Chronic conjunctivitis characterized by interpalpebral bulbar conjunctival hyperemia may be present, and cicatricial conjunctivitis involving the lower lid is one of the most common ocular surface findings in rosacea. Corneal manifestations, including keratitis and recurrent corneal epithelial erosions, may also occur in up to 33% of patients with rosacea.

Diagnosis

Ocular rosacea is diagnosed clinically, and laboratory studies are not implicated.

Differential Diagnosis

Staphylococcal and seborrheic blepharokeratoconjunctivitis; sebaceous gland carcinoma; cicatricial pemphigoid; allergic, bacterial, and viral conjunctivitis; corneal erosion; atopic dermatitis; dry eye syndrome; episcleritis; bacterial keratitis; atopic keratoconjunctivitis; sicca keratoconjunctivitis; corneal ulcer.

Prophylaxis

Broad spectrum sunscreen for photoprotection, regular eye exams.

Therapy

It is important to avoid trigger factors, which are highly individualized. Mild ocular rosacea requires

local remedies such as warm compresses, lid hygiene with neutral baby shampoo, and instillation of lubricating drops. Topical cyclosporine 0.05% can assist with tear production and quality. Antibiotic ointments applied nightly can decrease eyelid flora and help soften collarettes. Moderate ocular rosacea may require systemic treatment, such as tetracycline, doxycycline, or azithromycin, in addition to topical therapy. For persistent ocular inflammation, topical corticosteroids or cyclosporine has proven to be beneficial. However, due to the adverse side effects of long-term steroid use, such as glaucoma and cataracts, cyclosporine is preferable. Surgical intervention may be required in certain instances, such as chalazia, corneal thinning, and corneal perforations.

Prognosis

Prognosis depends on the severity of the condition.

Epidemiology

Out of the 10% of the general population, up to 60% experience ocular complications. Ocular rosacea affects both sexes equally.

Cross-References

- ▶ Blepharitis
- ▶ Blepharoconjunctivitis
- ▶ Chalazion

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Rosengren-Doane Tear Pump

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Synonyms

Lacrimal pump

Definition

A mechanism theorized by Rosengren-Doane thought to be responsible for the active excretion of the tears through the nasolacrimal drainage system.

Structure

The nasolacrimal system is comprised of multiple parts measuring approximately 32 mm in its entirety. There are two puncta, one at the medial aspect of each lid, approximately 5 mm from the medial canthus. They are apposed to the globe yet slightly inverted to allow them to rest in the tear lake. Each punctum is approximately 0.2 mm in diameter and surrounded by the ampulla perpendicular to the lid margin.

Each puncta ends in the canaliculi which course perpendicular to the lid margin approximately 2 mm before turning at a 90 angle medially. They then run approximately 8–10 mm before combining to form a common canaliculus in 90% of patients.

The tears then pass through the valve of Rosenmüller, a mucosal fold at the juncture of the common lacrimal canaliculus and superior aspect of the lacrimal sac (see "▶ Rosenmüller, Valve of"). The lacrimal sac extends for approximately 10 mm inferiorly within the bony fossa in the medial orbit. It is bordered by the anterior and posterior lacrimal crests.

The lacrimal sac then becomes the nasolacrimal duct extending inferiorly

approximately 12 mm and terminating in an ostium just beneath the inferior turbinate. This ostium is covered by another mucosal fold (the valve of Hasner).

Important to understanding the tear pump is the orientation of the orbicularis muscles. The pretarsal orbicularis is just anterior to the tarsus. Its fibers run horizontally and are the innermost ring of orbicularis tissue. Just surrounding the preseptal orbicularis is the preseptal orbicularis. The preseptal component overlies the orbital septum and originates from the superficial and deep heads of the medial canthal tendon. It has attachments to the lacrimal sac that contribute to the Rosengren-Doane tear pump mechanism.

Function

The Rosengren-Doane tear pump is the predominate theory of the active excretion of tears through the nasolacrimal system. In this theory, the pretarsal and preseptal orbicularis muscles work together to create concomitant positive and negative pressure propelling the tears from the tear lake into the nose.

At rest, when the eyelids are fully open, the puncta pop open, and the negative pressure allows the canaliculi to fill with tears. As the upper eyelid closes, both portions of the orbicularis contract. The horizontal fibers of the pretarsal orbicularis squeeze closed the canaliculi thus forcing the tears into the lacrimal sac and occluding the puncta to prevent reflux. The preseptal orbicularis attached to the lacrimal sac pulls the lacrimal sac laterally creating a negative pressure and allowing the tears to flow into the lacrimal sac. As the lid reopens and the orbicularis relaxes, the lacrimal sac then closes creating a positive pressure on the sac pushing the tears into the nasolacrimal duct and into the nose.

Clinical Relevance

Normal tear drainage relies on a fully functioning Rosengren-Doane tear pump. Understanding the active mechanism of active tear elimination and anatomy of the lacrimal system can help one appropriately diagnose and pinpoint diseases of this system.

Reduced drive to blink, incomplete blink, lid deformity, or involutional laxity can all contribute to malfunction of the lacrimal pump. This can result in epiphora or corneal exposure if not appropriately identified and treated.

Poor anatomic apposition of the puncta to the globe or punctal stenosis can lead to insufficient tear drainage into the canaliculi resulting in epiphora.

Infections of the nasolacrimal system (i.e., dacryocystitis or canaliculitis) can also cause obstruction and malformation.

Cross-References

▶ Trauma, Lacrimal Sac and Nasolacrimal Duct

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Rosenmüller Fold

▶ Rosenmüller, Valve of

Rosenmüller, Valve of

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Synonyms

Rosenmüller fold; Valve of Hanske

Definition

The valve of Rosenmüller is not a true valve, but rather a mucosal fold at the juncture of the common canaliculus and the lacrimal sac. It separates the palpebral portion of the lacrimal drainage system from the lacrimal sac and nasolacrimal duct. The valve of Rosenmüller is named after the German anatomist, Johann Christian Rosenmüller (May 25, 1771–February 28, 1820), who first described the structure.

Structure

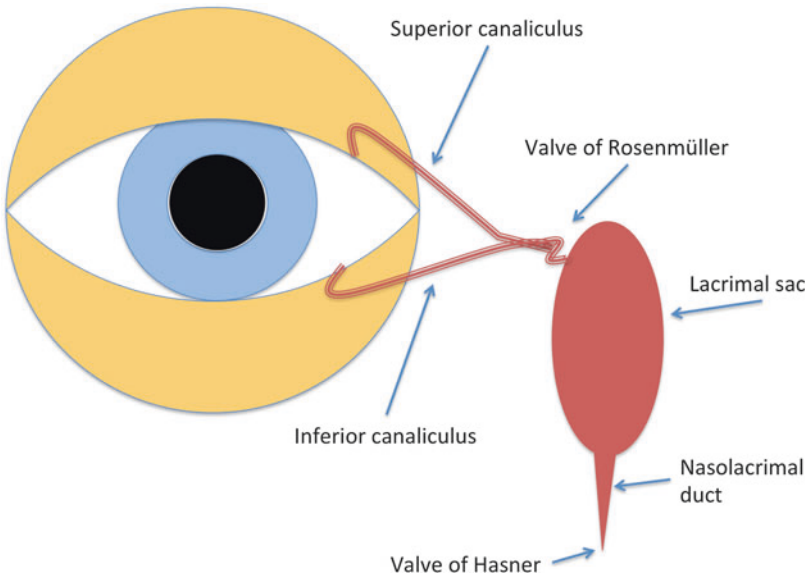
The valve of Rosenmüller is a mucosal fold at the juncture of the common lacrimal canaliculus and the superior aspect of the lacrimal sac (Fig. 1). According to cadaveric studies, there is a consistent pattern of angulation within the canalicular system. The canaliculi bend first posteriorly as they travel behind the medial canthal tendon and then bend anteriorly at an acute angle to enter the lacrimal sac (Tucker et al. 1996). This pattern of bending is consistently observed in a majority of specimens, and a mucosal fold corresponding to the valve of Rosemüller is observed in approximately 60% of persons (Zoumalan et al. 2011).

Function

Lacrimal drainage must transit the valve of Rosenmüller from the common canaliculus to the lacrimal sac and nasolacrimal duct. The physiologic role of the valve of Rosenmüller is to prevent reflux of tears from the lacrimal sac into the canalicular system. It is postulated that the fold of tissue functions as a one-way valve to enable flow from the common canaliculus into the lacrimal sac, but preventing retrograde flow (American Academy of Ophthalmology 2015).

Clinical Relevance

In lacrimal probing, the valve of Rosenmüller is felt as a "soft stop" as the probe is advanced through the common canaliculus and into the lacrimal sac, prior to the "hard stop" felt as the probe contacts the bony lacrimal fossa (Schmidt 1996).



Rosenmüller, Valve of, Fig. 1 Schematic of nasolacrimal anatomy

On punctal irrigation for the evaluation of potential nasolacrimal obstruction, an obstruction at the level of the valve of Rosenmüller will cause reflux of the irrigated saline out of the opposite punctum.

In dacryocystitis or nasolacrimal duct obstruction, palpation or massage over the lacrimal sac may produce reflux if the valve of Rosenmüller and canalicular system are patent (Cohen et al. 2014).

A dacryocystocele requires blockage of the valve of Rosenmüller proximally as well obstrcution of the nasolacrimal duct distally in order to form a cystic enlargement of the lacrimal sac (Cohen et al. 2014).

In dacryorhinocystostomy (DCR) surgery, the adherent mucosal tissue forming the valve of Rosenmüller may need to be excised if causing an obstruction at the entrance to the lacrimal sac (Cohen et al. 2014).

Cross-References

- ▶ Canaliculitis
- ▶ Trauma, Lacrimal Sac and Nasolacrimal Duct

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Rosenthal Syndrome

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Synonyms

Miescher-Melkersson-Rosenthal syndrome

Definition

Melkersson-Rosenthal syndrome (MRS) was first described by Melkersson in 1928. MRS is characterized by the clinical triad of recurrent swelling, facial nerve palsy, and fissured tongue.

Etiology

While the exact etiology for MRS is unknown, it has been postulated to be associated with adverse

reactions to infection, allergy, or foreign material such a silicates, gold, and mercury; more recently, it has been theorized to have hereditary occurrence and genetic predisposition (autosomal dominant, locus: 9p11) (Gorlin et al. 1990; Laskaris 2003).

Clinical Presentation

Symptoms and signs of MRS include unilateral/bilateral facial paralysis, gingival edema, fissured tongue, and chronic and recurrent facial swelling in regions of face, lips, palate, cheeks, and tongue. MRS has also been associated with migraine, megacolon, and stress, implicating vasomotor instability and autonomic dysfunction (Laskaris 2003; Weedon et al. 2010).

Diagnosis

The diagnosis of MRS can be confirmed by characteristic biopsy showing noncaseating granulomas and/or lymphedematous alteration (Laskaris and George 2005; Grewal and Grewal 2012).

Differential Diagnosis

Hughes syndrome, Crohn disease, sarcoidosis, cheilitis granulomatosa, tuberculosis, angioneurotic edema, and allergic gingivostomatitis.

Therapy

Treatment of this syndrome is symptomatic, targeted toward therapy of facial palsy and correction of facial disfigurement due to edema. Facial palsy is managed by warm compresses, analgesics, oral corticosteroids, antibiotic eye drops, and ointment and usually recovers completely; however recurrences may occur. Facial decompression has been used in severe cases. Recent advances in therapeutic modalities have broadened to include the use of laser beam acupuncture and oral clofazimine to reduce swelling and avoid permanence (Laskaris and George 2005; Grewal and Grewal 2012).

Prognosis

MRS may recur or progress and may develop into a chronic disorder.

Epidemiology

MRS has been found in childhood or early adolescence and is three times more common in females than males but affects less than 200,000 people in the USA (Gorlin et al. 1990).

Cross-References

▶ Facial Nerve Palsy

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Rotational Advancement Flap

▶ Z-Plasties

Rotational Flap for Eyelid Repair

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Synonyms

Mustarde rotational flap; Simple rotational flap

Definition

A technique utilized in eyelid repair surgery to reconstruct a defect in the anterior lamellar (skin and muscle) of the eyelid, in which tissue from an area of relative excess is rotated in an arc around a fixed pivot point to fill the defect.

Indication

Rotational flaps are indicated for the repair of anterior lamellar deficiencies of the eyelid (typically the lower eyelid) in which there is inadequate tissue available for direct simple closure. These defects are most commonly secondary to cancer resection surgery, including Mohs surgery, and trauma. The rotational flap can redirect tension on the wound into the horizontal as opposed to the vertical plane, thereby minimizing the risk of eyelid malpositions, particularly ectropion.

Contraindications

In trauma patients, surgery should be deferred until the patient is stable and a suitable candidate for surgery. Also more serious injuries, such as a ruptured globe, take precedence and should be repaired prior to the eyelids. The donor tissue to be transposed must be healthy and viable.

Techniques and Principles

In planning the appropriate design and orientation of the rotational flap the surgeon carefully considers the degree of local skin mobility and the orientation of relaxed skin tension lines, which will result in the least conspicuous scar. In general tissue is transposed from an area of relative excess to an area with insufficient tissue to allow closure. The rotational flap, particularly when used in the lower eyelid, can also be utilized to redirect tension on the wound into the horizontal as opposed to the vertical plane, thereby minimizing the risk of eyelid malpositions, particularly ectropion. The incision is created and the tissue undermined until arcuate advancement can be achieved to fill the defect. Very large lower eyelid defects can be reconstructed with an extensive Mustarde rotational flap.

Outcome

Rotational flaps allow for recruitment of vascularized anterior lamellar tissues (skin and muscle) for reconstruction of eyelid defects. The desired result is a functional eyelid, which can provide adequate protection of the globe. The resultant scar is semicircular in shape.

Complications

Any excess tension on the flap can result in wound dehiscence or flap necrosis. Eyelid malpositions including ectropion or entropion are possible, particularly with tension on the wound closure or exuberant wound contraction and fibrosis.

Cross-References

▶ Eyelid Reconstruction
▶ Mustarde Flap

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RPE

► Retinal Pigment Epithelium

Ruptured Globe

► Corneoscleral Laceration

Rust Ring

► Iron, Corneal Intraocular Foreign Body of

Rust Ring, Iron Foreign Body Causing

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Synonyms

Direct siderosis

Definition

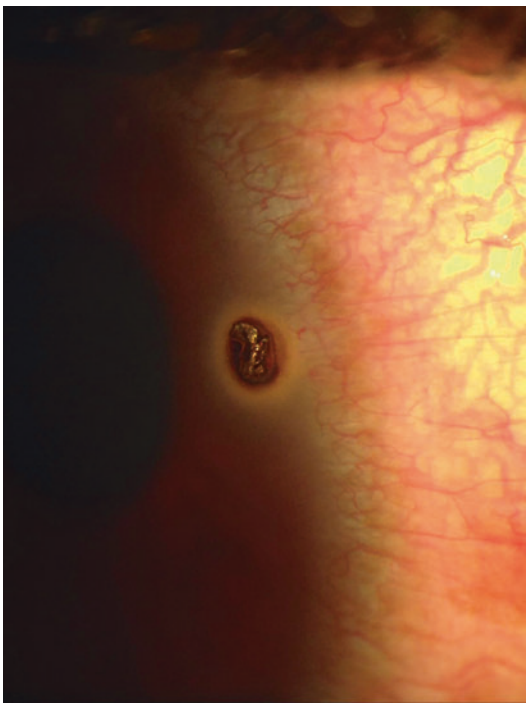
The product of an immune reaction produced by an oxidized iron foreign body in the cornea. Typically formed within 3–4 h after the introduction of the ferrous body (Brock and Gurekas 2013). Clinically identified as a reddish brown circular opacity confined to Bowman's layer or anterior stroma. Necrotic corneal tissue can be removed with the use of a burr or small gauge needle (McGuinness and Knight-Jones 1968).

Etiology

Immune product from an oxidized iron foreign body in the cornea (Zuckerman and Lieberman 1960).

Occurrence

A corneal rust ring typically develops 3–4 h after the iron foreign body is introduced in the cornea (Fig. 1). Corneal foreign bodies are very common eye injuries in workers dealing with metallic objects and high speed drills and



Rust Ring, Iron Foreign Body Causing, Fig. 1 Iron foreign body

grinders. They are the most common industrial ocular accident. The majority of corneal foreign bodies are centrally located and can leave a residual scar in the patient's visual axis (Tasman and Jaeger 2001). The presence of iron particles within the cornea causes localized tissue necrosis which is typically removed in order to facilitate wound healing (Brown et al. 1975). Incomplete removal of necrotic tissue should be suspected when delayed epithelialization, chronic foreign body sensation, and extended light sensitivity follow the removal of a corneal metallic foreign body.

Classification

Immune-mediated reaction
Oxidation reaction to ferrous foreign body

Cross-References

- ▶ Intraorbital Foreign Body (IOFB)
- ▶ Penetrating Eyelid Injuries
- ▶ Siderosis

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S

Saccadic Nystagmus

► Flutter, Ocular

Sakurai-Lisch Nodules

► Lisch Nodules, in Neurofibromatosis

Salzmann Nodular Degeneration

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Definition

Salzmann's nodular degeneration is a slowly progressive, degenerative condition of the cornea that is rare, noninflammatory, and characterized by bluish-white nodules on the corneal surface.

Etiology

The disease can be idiopathic, but often times, it is from chronic ocular surface irritation and associated with preexisting corneal diseases. It often presents in patients with a history of keratitis, most commonly trachomatous or phlyctenular, but also in vernal or other forms of keratitis caused by scarlet fever, measles, and uveitis (Das et al. 2005). Other associations include epithelial basement membrane dystrophy, Thygeson's punctate keratitis, postcorneal surgery, keratoconus, contact lens, and ocular trauma.

Clinical Presentation

Salzmann nodules are bluish-white-to-gray subepithelial nodules that tend to develop slowly (Das et al. 2005). They are usually round prominences, but can be conical or elongated, often less than 2 mm, but can be as large as 4 mm or more. They usually number between 1 and 8 and can be distributed on any part of the cornea. The nodules may or may not be vascularized. They may affect vision by direct obstruction of visual axis or by induced spherical or astigmatic error. They are associated with iron-containing line and negative fluoresce in staining or pooling at the base of the nodule.

Diagnosis

Diagnosis of Salzmann nodules is based on the clinical exam. Examination is primarily based on the slit-lamp biomicroscopy, but should also include keratometry and corneal topography to record surface irregularity. Histologically, the epithelium cells show degenerative change,

10.1007/978-3-540-69000-9_100703"

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including epithelial cells that have flattened and basal cells that have lost their columnar shape and contain degenerative vacuoles and clumped nuclear chromatin. The bowman's layer could be absent and replaced by granular PAS-positive eosinophilic material (Das et al. 2005). Hyaline plaques have also been found between the corneal epithelium and Bowman's layer.

Differential Diagnosis

Bullous keratopathy
Climatic droplet keratopathy
Corneal amyloidosis
Corneal keloid
Hereditary hypertrophic scarring
Pterygoid corneal dystrophy

Therapy

Treatment is not necessary if the patient is asymptomatic. Asymptomatic patients are mostly those with nodules limited to the peripheral cornea. For mild irritation, lubrication is recommended. Surgical intervention should be considered in patients who have nodules that exhibit growth, decrease in surface regularity, and loss of visual acuity. In cases where the nodule is easily separated manually from the corneal surface and does not involve Bowman's layer, recurrence rates are low. If lesions involve Bowman's layer and superficial stroma, phototherapeutic keratectomy should be considered for surface irregularities. Manual removal methods have included using forceps to grasp and strip them from the surface of the cornea, using a Graefe's knife or no. 15 blade to perform a superficial excision, or a trephine to remove the base of the nodules and reach clear cornea. Cryotherapy has been used previously. Cauterization has also been used but may induce corneal opacification. Amniotic membrane transplantation may help with reducing inflammation, scarring, and vascularization after a superficial keratectomy. Recurrences may warrant superficial keratectomy or phototherapeutic keratectomy with application of mitomycin C. One study that looked at 30 eyes that underwent superficial keratectomy and mitomycin C found no recurrence during a mean follow-up of 28 months. Visual acuity and corneal clarity may improve in some patients after treatment. Lamellar or penetrating keratoplasty may be needed for lesions that extend to the mid-stroma. Though recurrences have been reported after penetrating keratoplasty, it is hardly ever needed (Bowers et al. 2003).

Prognosis

The disease is slowly progressive, with most patients not being aware of their disease beginning. In about 60% of eyes, the nodules are located in the paracentral and central areas. Surgical removal has been shown to be effective, and application of mitomycin C has helped reduce reoccurrences (see "Therapy" above). One study has reported up to almost three lines of visual acuity improvement after PTK (Maloney et al. 1996).

Epidemiology

Salzmann nodular degeneration has been reported more commonly in white, elderly, and female persons (Das et al. 2005). The disease is more often unilateral. However, it has been seen in patients of different ages, races, and gender and can be bilateral.

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Sarcoid

► Sarcoidosis

Sarcoidosis

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Synonyms

Sarcoid

Definition

Sarcoidosis is a non-caseating granulomatous inflammatory disorder mediated by T-lymphocytes. Its exact cause has not been elucidated. Sarcoidosis can range from affecting a single organ to being a fatal multiple system disease. Most often, mediastinal lymph nodes, lungs, liver, parotid glands, spleen, skin, and the eye are affected.

Etiology

The cause of sarcoidosis is unknown. The disease process involves T-cell-mediated granulomatous inflammation.

Clinical Presentation

Sarcoidosis can have an acute or insidious onset. Two syndromes, Lofgren syndrome and Heerfordt syndrome, are known to present acutely in young patients. In Lofgren syndrome, patients present with erythema nodosum and bilateral hilar lymphadenopathy that is also associated with fever, arthralgia, and anorexia. In Heerfordt syndrome, also known as uveoparotid fever, patients present with uveitis, fever, parotitis, and cranial nerve palsy, usually involving the seventh cranial nerve.

In insidious onset sarcoidosis, the disease can present skin lesions, pulmonary disease, and other less common manifestations such as neurological disease, arthritis, bone cysts, renal disease, lymphadenopathy, splenomegaly, glaucomatous liver disease, and cardiac arrhythmias. Pulmonary disease can manifest as bilateral asymptomatic hilar lymphadenopathy, diffuse reticulonodular infiltrates, or even pulmonary fibrosis which may result in pulmonary hypertension and cor pulmonale. In 25% of patients, skin lesions may manifest as erythematic nodosum, glaucomatous scattered plaques or nodules, lupus pernio, or glaucomatous deposits in long-standing scars. In 5–10% of patients, sarcoidosis may result in a unilateral facial nerve palsy. More rare neurological manifestations include meningitis, seizures, peripheral neuropathy, and psychiatric symptoms. In chronic sarcoidosis, patients may experience arthritis of the large and small joints. This can be confused with juvenile idiopathic arthritis in children because in the young, sarcoidosis is more likely to present as an arthropathy than with pulmonary findings. Renal disease can manifest as nephrocalcinosis.

There are a myriad of ways that sarcoidosis presents affecting the eye. The most common is uveitis which can be anterior, intermediate, or posterior in nature. Other ocular manifestations include keratoconjunctivitis sicca, conjunctival nodules, and, very rarely, scleral or orbital lesions. Patients can have an acute anterior uveitis or a chronic granulomatous which typically affects older patients with pulmonary disease. These patients can also have nodules of the iris or even trabecular meshwork. Sarcoidosis patients with intermediate uveitis may present with snowballs. Other patients may have periphlebitis which would appear as yellowish or gray-white perivenous sheathing which can sometimes also involve the optic nerve. Severe periphlebitis will result in perivenous exudates called candlewax dripping nodules. Other manifestations include KCS, conjunctival nodules, and, rarely, orbital and scleral lesions. Although rare, choroidal infiltrates can present as many small, pale yellow "punched-

out" infiltrates, multiple large confluent lesions with amoeboid margins, or exceedingly rarely as solitary choroidal granulomas. When sarcoidosis present as multifocal choroiditis, visual prognosis is poor. This is because choroidal neovascularization may result in loss of central vision or a chorioretinal scar. Other ocular findings can include retinal granulomas, peripheral retinal neovascularization secondary to retinal capillary dropout, a nummular keratitis, and optic nerve involvement. Optic nerve involvement could include focal granulomas by the optic nerve, papilledema secondary to central nervous system involvement, or persistent disk edema associated with vitreous or retinal involvement.

Diagnosis

Without histologic confirmation, sarcoidosis is a diagnosis of exclusion. Enzyme assays of angiotensin-converting enzyme (ACE) and lysozyme levels in addition to biopsy are common methods used to assess for sarcoidosis. Lung biopsy is the highest yield (90%). This is so even in asymptomatic patients with a normal chest X-ray. In patients with conjunctivitis with conjunctival nodules, biopsies are positive 70% of the time. In enlarged lacrimal glands, biopsies are positive 75% of the time, but in un-enlarged lacrimal glands, biopsy yield can be as low as 25%. Pulmonary function tests would show a restrictive lung disease pattern. A strongly positive Mantoux test to a tuberculin unit would make a diagnosis of sarcoidosis less likely. Chest radiographs will be abnormal 90% of the time.

Differential Diagnosis

The differential diagnosis of posterior segment sarcoidosis is organized into small choroidal lesions, large choroidal infiltrates, and periphlebitis. Small choroidal lesions could also be tuberculosis, birdshot chorioretinopathy, or multifocal choroiditis with panuveitis. Findings of large choroidal infiltrates could also be large cell lymphoma, Harada disease, serpiginous choroidopathy, or metastatic tumor. Finally, other causes of periphlebitis could be Behcet syndrome, tuberculosis, or cytomegalovirus retinitis.

Prophylaxis

There is no prophylaxis for this disease.

Therapy

Therapy for anterior uveitis is topical and/or periocular steroids. On the other hand, posterior uveitis may require systemic steroids or immunosuppressive agents such as methotrexate, cyclosporine, or azathioprine. Cyclophosphamide has been shown to be useful in refractory disease as well as infliximab.

Prognosis

Prognosis is generally good if patient has timely diagnosis and treatment. However, in cases of multifocal choroiditis, visual prognosis is especially guarded as the patient may develop choroidal neovascularization resulting in loss of central vision or a chorioretinal scar.

Epidemiology

Sarcoidosis more commonly affects patients of African than Caucasian descent. It is also more frequently found in colder climates.

Cross-References

▶ Heerfordt's Syndrome

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Sarcoidosis, Orbit Affected in

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Definition

Sarcoidosis is a multisystem autoimmune disease with manifold features. The name sarcoid is derived from the Greek root *sarx* – meaning flesh – and sarcoidosis is so-named because the characteristic granulomas seen in sarcoidosis have a fleshy consistency.

Basic Characteristics

Clinical Features

Sarcoidosis is considered one of the "great imitators" in human disease and may present with protean features. The characteristic lesion in sarcoidosis is the noncaseating granuloma.

Any organ system can be affected, but the chest is most commonly involved and pulmonary nodules are seen in 90% of cases. Sarcoidosis may involve any part of the orbit and any part of the eye itself. Anterior uveitis is the most common ocular finding. Orbital involvement is present in 8–10% of patients with sarcoidosis (Demirci 2015). Within the orbit, the lacrimal gland is the most common orbital site, with up to 60–80% of patients demonstrating lacrimal gland involvement on gallium scanning. Other orbital tissues are rarely involved but may include the extraocular muscles and the optic nerve.

Presentation

Exam findings in orbital sarcoidosis include palpable mass or palpable lacrimal gland enlargement, proptosis, diplopia, pain, ptosis, limited ocular motility, and ocular irritation. Lacrimal gland inflammation may present symptoms of dry eye or with an enlarged lacrimal gland. Within the orbit, the lacrimal gland is the most commonly affected site, (42%) followed by orbital fat/soft tissue (39%), eyelids (12%), and lacrimal sac (8%) (Demirci 2015; Black and Smith 2012).

Epidemiology

While sarcoidosis may affect persons of all ages and races, most cases are diagnosed between the ages of 20 and 40. In the United States, sarcoidosis most commonly affects African-Americans, but high rates are also found in Ireland and in Scandinavia. In the United States, the incidence is 3–10 per 100,000 for Caucasians and 35–80 per 100,000 for African-Americans. In the ACCESS (A Case Control Etiologic Study of Sarcoidosis), which included 706 newly diagnosed patients, ocular involvement was more common in African-Americans than in Caucasians (Demirci 2015; Black and Smith 2012).

Diagnosis

Diagnostic testing for sarcoidosis may include chest radiographs or chest CT to evaluate for pulmonary nodules. Orbital imaging demonstrates diffuse homogenous or lobular enlargement and enhancement of the lacrimal gland. Serum assays include ACE and calcium levels, complete blood counts, and complete metabolic panel and a chest X-ray for hilar lymphadenopathy. Conjunctival biopsy may be helpful in the diagnosis of systemic sarcoidosis, but biopsies of clinically or radiographically significant nodules have a higher yield. The defining characteristic of sarcoidosis on histology is the noncaseating granuloma. Biopsy of affected tissues is diagnostic. Lacrimal gland biopsy is often diagnostic for orbital involvement, and lesions demonstrate the typical noncaseating granuloma.

Management

Potent anti-inflammatory or immunosuppressive medications are the mainstay of treatment for sarcoidosis. Corticosteroids are typically used in the acute phase, and steroid-sparing agents such as azathioprine, methotrexate, and plaquenil are used for chronic therapy. In localized orbital disease, periocular injections of triamcinolone may be used.

Cross-References

- ▶ Biopsy
- ▶ Orbit, Inflammation of
- ▶ T1 Magnetic Resonance Image (MRI)
- ▶ Three-Dimensional Computed Tomography, in Orbital Evaluation

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Sarcoma, Orbital

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Synonyms

Malignant mesenchymal tumor of orbit

Definition

Sarcomas are malignant soft tissue tumors of mesenchymal origin. Derived from the Greek root word *sarx*, meaning "flesh," the term sarcoma refers to a variety of malignancies derived from soft tissues, including cartilage (chondrosarcoma), bone (osteosarcoma, Ewing sarcoma), connective tissue (fibrous histiocytoma, alveolar sarcoma), muscle (leiomyosarcoma), and fat (liposarcoma). Sarcomas are rare but aggressive tumors and may affect the orbit.

Etiology

A variety of sarcomas may affect the orbit, all of which are rare, accounting for less than 1% of all orbital malignant tumors. Orbital sarcomas include malignant tumors of bone (osteosarcoma, Ewing sarcoma), connective tissue (fibrous histiocytoma, alveolar sarcoma), muscle (leiomyosarcoma), and fat (liposarcoma).

Osteosarcoma is the most common malignant bone tumor overall, but orbital involvement is rare, and these comprise only 0.5–1% of orbital tumors. Osteosarcoma arises from mesenchymal bone precursor cells and can occur in any bone, usually the metaphyseal plates of the long bones. Typically orbital involvement occurs secondarily, as a result of invasion from the adjacent paranasal sinuses, although metastases from distant sites have also been reported. Most tumors arise de novo, but osteosarcoma may also arise in the setting of dysplastic bone growth, such as Paget's disease, fibrous dysplasia, or prior radiation therapy. Osteosarcoma is known to occur as a second malignancy in patients with familial retinoblastoma who have undergone orbital radiotherapy for retinoblastoma (Perry and Singh 2013). Approximately 10% of patients with osteosarcoma have a history of prior radiotherapy to the affected area, and similarly, retinoblastoma patients undergoing radiotherapy have approximately a 10% risk of developing osteosarcoma by age 25 (Black and Smith 2012).

Ewing sarcoma is a malignant tumor of bone that occurs most commonly in younger patients, with 75% aged 20 or younger and 90% aged 30 or younger at the time of presentation. Ewing sarcoma is classically a tumor of the long bones, and orbital involvement typically occurs secondarily as a result of metastatic spread (Esmaeli 2010).

Fibrous histiocytoma is the most common mesenchymal tumor in adults. Malignant fibrous histiocytoma or myxofibrosarcoma may arise de novo, as a primary malignancy or as a secondary malignancy following orbital radiation for retinoblastoma, especially in patients with germline mutations. Malignant fibrous histiocytomas are aggressive tumors and require orbital exenteration. Distant metastases are rare but local recurrence and local infiltrative disease are common (Perry and Singh 2013).

Leiomyosarcomas, malignant tumors of smooth muscle, are seen most often after orbital

radiotherapy in children, such as orbital radiation for retinoblastoma. Smooth muscle origins for these tumors include perivascular smooth muscle, Muller's muscle, and precursor cells (Perry and Singh 2013).

Liposarcoma is common in adults, but very rarely occurs within the orbit. Orbital involvement may occur in the setting of disseminated metastases (Perry and Singh 2013).

Clinical Presentation

Orbital sarcomas may present similarly to orbital inflammatory disease or orbital infection, with "orbital signs" including pain, proptosis, periocular edema, and limited extraocular movement and signs of optic nerve dysfunction such as decreased visual acuity, dyschromatopsia, or an afferent pupillary deficit. Depending on the location of the lesion, sensory nerve paresthesia may occur. Anteriorly located masses may be palpable on physical exam. Malignant lesions often progress insidiously over weeks or months, but may also present acutely with rapid development of pain, proptosis, and globe indentation or displacement. Overall, the most common presenting symptoms are proptosis, globe displacement, and diplopia.

Orbital involvement is typically secondary to systemic disease, and patients often have systemic symptoms of metastatic disease at the time of diagnosis, including fever, weight loss, and anorexia (Esmaeli 2010; Perry and Singh 2013; Black and Smith 2012).

Diagnosis

In addition to clinical history and physical examination, imaging is essential in the workup and diagnosis of orbital sarcomas. Dedicated CT or MRI of the orbit is indicated to assess mass location and extension and may help distinguish mass lesions from infectious disease. Orbital involvement is usually secondary to systemic malignancy or metastatic disease, and appropriate workup with an oncologist is indicated and may include PET-CT. A variety of orbital mass lesions may have a similar clinical presentation, and biopsy is required for definitive histopathologic diagnosis. Immunohistochemistry and flow cytometry techniques aid in diagnosis through the use of specific tumor markers. Characteristic imaging and histopathologic findings for several types of sarcoma are discussed below.

Osteosarcoma is visualized on CT imaging as a mixed lytic and sclerotic mass with irregular margins and tissue invasion and destruction. Lesion density may vary depending on the relative proportion of osseous, cartilaginous, and fibrous elements. Calcified areas and areas of dense osteoid appear bright on CT, but areas of fibrovascular proliferation appear darker than bone. There is marked enhancement with CT contrast. MRI is preferred for evaluation of soft tissue and demonstrates a lesion that is hyperintense on T1 and hypointense on T2 relative to muscle. Surrounding tissue edema may make the tumor appear larger on STIR sequences. There is heterogenous enhancement of the lesion with gadolinium.

The defining characteristic of osteosarcoma on histopathology is the production of malignant osteoid. Osteosarcoma arises from mesenchymal bone-forming precursors, and histopathology demonstrates osteoblastic, chrondroblastic, and fibroblastic malignant cells. On sectioning, islands of osteoid are surrounded by sheets of atypical osteoblasts. Areas of necrosis, calcification, and vascular proliferation may be seen (Black and Smith 2012).

Ewing sarcoma appears as an irregular, extraosseous mass on CT imaging with mottling and destruction of adjacent bone. There is variable enhancement with iodinated contrast, and necrotic or hemorrhagic areas appear hypodense. MRI similarly demonstrates an extraosseous mass with adjacent bony destruction. On T1 sequences, Ewing sarcoma is hypointense to muscle, whereas, on T2 sequences, the lesion appears hyperintense to muscle. Fat-suppressed sequences may be useful as the lesion appears isointense to fat on T2-weighted MRI. There is heterogenous enhancement with gadolinium with areas of necrosis appearing darker (Esmaeli 2010). Immunohistochemistry is an essential tool for diagnosis and can be used to detect expression of the EWS or MIC2 genes in Ewing sarcoma.

CT imaging of alveolar sarcoma demonstrates a well-defined mass most frequently involving the superior orbit. These lesions are highly vascularized, and consequently they demonstrate avid enhancement. Necrotic areas within the center of the tumor may appear dark. On histopathology, alveolar sarcoma appears with many large, polygonal cells with large nuclei and prominent nucleoli (Perry and Singh 2013).

Leiomyosarcoma: On CT, leiomyosarcoma appears as a well-defined, heterogenous, multilobed mass. The lesion may demonstrate molding to the contours of the globe and destruction of adjacent bone. Histopathology demonstrates multinucleated giant cells within the tumor (Perry and Singh 2013).

Liposarcoma may appear like a cyst, containing fat surrounded by a dense pseudocapsule. MRI will demonstrate hyperintense signal on T1 consistent with a fat-containing lesion (Perry and Singh 2013).

Differential Diagnosis

See Table 1.

Sarcoma, Orbital, Table 1 Differential diagnosis of orbital sarcoma

Infectious	Bacterial orbital cellulitis Fungi (aspergillosis, mucormycosis) Mycobacteria (tuberculosis) Parasites (i.e., hydatid cyst)
Noninfectious/ inflammatory	Idiopathic orbital inflammation (orbital pseudotumor) Thyroid eye disease Sarcoidosis Granulomatosis and polyangiitis Churg-Strauss Scleritis
Neoplastic	Metastatic disease Rhabdomyosarcoma Lymphoma Leukemia Extension of intraocular tumors (retinoblastoma, ocular melanoma) or periocular tumors (nasopharyngeal cancers, etc.)
Vascular	Cavernous sinus thrombosis Carotid-cavernous fistula Lymphangioma Cavernous hemangioma
Other	Trauma Ruptured dermoid Hematoma Orbital foreign body

Adapted from Black and Smith (2012), p. 936

Prophylaxis

Given the high rate of orbital osteosarcoma following orbital radiation, especially in children undergoing radiotherapy for retinoblastoma, surveillance with appropriate imaging should be performed in these patients.

Therapy

Surgical excision and radiotherapy are the standard treatment (Karcioglu 2014). Combination chemotherapy had been demonstrated to be effective for orbital sarcomas. Owing to the rarity and varied histology of orbital sarcomas, it is difficult to study treatment regimens prospectively, and there is limited evidence to support a particular treatment regimen. Combination chemotherapy has been used successfully and has been shown to be effective for the treatment of orbital sarcomas. Treatment of specific tumor types is described below.

Ewing sarcoma: Ewing sarcoma involving the orbit is considered a manifestation of systemic disease and is treated with systemic multi-agent chemotherapy. Chemotherapy regimens include combinations of vincristine, doxorubicin, cyclophosphamide, and dactinomycin. Following neo-adjuvant chemotherapy, definitive treatment is either surgical excision or radiation followed by adjuvant chemotherapy. Following treatment, patients are followed closely for recurrences (Esmaeli 2010).

Alveolar soft part sarcoma: For alveolar sarcoma, surgical resection with wide margins is required and may include orbital exenteration for recurrent or aggressive disease. The role of chemotherapy and radiation is unknown (Perry and Singh 2013).

Osteosarcoma: Osteosarcoma is managed surgically with preoperative and postoperative chemotherapy. Multi-agent regimens are utilized and may include methotrexate, dacarbazine, cyclophosphamide, doxorubicin, or cisplatin. Radiation is also used as an adjunctive treatment and is especially useful for patients with residual tumor or unresectable tumors (Black and Smith 2012).

Leiomyosarcoma: Leiomyosarcoma is an aggressive tumor with 60% recurrence within 3 years after local resection. Most cases require extended orbital exenteration with wide margins, including adjacent bones. Treatment may include systemic chemotherapy and adjunctive local radiotherapy (Perry and Singh 2013, p. 144).

Liposarcoma: Well-differentiated tumors may be treated with local resection and adjuvant radiation. Metastases from orbital disease are uncommon (Perry and Singh 2013).

Prognosis

Treatment outcomes for orbital sarcoma vary depending on tumor type and extent at the time of diagnosis. The prognosis for localized orbital tumors is generally more favorable than for patients with disseminated disease.

Ewing sarcoma treated with multimodal therapy has a 5-year survival of approximately 65% for patients with localized disease. Metastases portend a poor prognosis, with only a 25% 5-year survival rate (Esmaeli 2010).

Alveolar soft part sarcoma limited to the orbit carries a relatively good prognosis, with 10-year survival approaching 85%. Disease involving the lower extremities carries a worse prognosis (Perry and Singh 2013).

Orbital osteosarcoma carries a poor prognosis with a 5-year survival of approximately 10% (Perry and Singh 2013; Black and Smith 2012).

Epidemiology

Sarcomas are very rare malignancies of the orbit. The most common orbital sarcomas in adults are malignant fibrous histiocytoma, hemangiopericytoma, fibrosarcoma, malignant peripheral nerve sheath, chondrosarcoma, and liposarcoma, each of which accounts for less than 1% of all orbital tumors (Karcioglu 2014). Typical age at presentation varies depending on tumor type. Osteosarcoma is the most common mesenchymal tumor of the orbit in children, whereas fibrous histiocytoma is the most common in adults.

Osteosarcomas have been associated with fibrous dysplasia, Paget's disease, and prior radiotherapy. Approximately 10% of patients with orbital osteosarcoma have a history of prior radiation to the orbit. Familial retinoblastoma is also associated with orbital osteosarcoma, and patients with germline mutations carry a 10% risk of developing osteosarcoma by age 25. Ewing sarcoma primarily affects young patients with 90% of cases occurring before age 30 (Esmaeli 2010; Perry and Singh 2013).

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Sattler's Veil (Central Epithelial Edema)

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Synonyms

Central corneal clouding; Central epithelial edema

Definition

Sattler's veil is defined as acute, central, intracellular microcystic epithelial edema. This edema often results in minor ensuing blurry vision caused by contact lens wear.

Etiology

Sattler's veil occurs secondary to acute hypoxic effects on the central corneal epithelium and is usually associated with tight-fitting rigid gas permeable or hydrogel contact lens wear. Vision is decreased when light is diffracted in the swollen epithelium. The central cornea presents with a distinct frosted glass appearance and is separated from the peripheral cornea with a clear zone. However, a diffuse haze may occur across the entire epithelium if the hypoxia is caused by tight-fitting hydrogel lenses.

Occurrence

The occurrence of Sattler's veil has decreased with the advent of better fitting hydrogel contact lenses.

Classification

Iatrogenic self-limiting disease (reversible upon cessation of contact lens wear).

Cross-References

► Bifocal Lenses

Further Reading

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Scanning Confocal Microscope

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Synonyms

Confocal microscope

Definition

The confocal microscope is an imaging instrument, first described by Minsky in 1957, designed to improve optical resolution up to 1–2 μm laterally by focusing both the light source and observation system on the same single point, hence the term confocal. Since the field of view is quite limited with a point source of light, a scanning confocal microscope was developed to rapidly scan the focal point over a larger area and create a real-time image (Jalbert et al. 2003; Guthoff et al. 2009). In vivo scanning confocal microscopy is the use of a scanning confocal microscope to view tissues in a living subject at high resolution without the need for tissue resection (Jalbert et al. 2003).

Purpose

The scanning confocal microscope is used in basic science research when high magnification is needed to view samples, since it has improved resolution when compared with light microscopes. Initially, confocal microscopes were used solely for basic science research, but have been transitioned for clinical usage. Using the same principle of confocality, high-resolution cellular-level images of living tissues can also

be taken in a clinic setting. This is called in vivo scanning confocal microscopy (IV SCM). In the field of ophthalmology, in vivo scanning confocal microscopy allows for noninvasive images with microns of resolution of eye structures, such as the cornea, conjunctiva, and lid margin (Guthoff et al. 2006).

Principle

The basic configuration of a confocal microscope consists of a pinpoint light source that is focused onto a point on the specimen (Guthoff et al. 2009). The type and shape of the light source are different depending on the type of confocal microscope. The light reflected from the specimen is collected by a lens and passed on to a beam splitter. The deflected light then enters a photodetection device though a conjugate pinhole, suppressing light originating from outside the focal point. The photodetection device converts the light signal into an electrical signal, which can be read and interpreted by software into an image. There are three main types of scanning confocal microscopes which are described below: tandem scanning confocal microscopes, slit scanning confocal microscopes, and laser scanning confocal microscopes. Newer generations of confocal microscopes are basically changing the light source to a less intense and more coherent light source (white light vs. single nanometer wavelength light) in order to attain cleaner images. With each successive generation of confocal microscope, the axial (z axis) resolution improves making the images much clearer. The scanning confocal microscope can also be used for contact or noncontact microscopy (Jalbert et al. 2003).

Tandem Scanning Confocal Microscope

The tandem scanning confocal microscope (TSCM) uses a spinning Nipkow disk, which is a metal plate with pinholes arranged in a spiral. The pinholes allow for multiple point illuminations at a single time, and the rapid rotation of the disk provides quick scanning of the specimen (Guthoff et al. 2009). The TSCM provides real-time images with true color; however, the image quality is marginal as the reflected light is low in intensity. Because the reflected light is low in intensity, the TSCM requires a very bright illuminating source such as a xenon or mercury arc lamp. Two companies developed a clinical version of this microscope, which is no longer in production. The lateral resolution (x-y axis) has been reported as 0.5–1.0 μm, and the axial resolution (z axis) has been reported as 9–11 μm using the TSCM (Jalbert et al. 2003).

Slit Scanning Confocal Microscope

The slit scanning confocal microscope (SSCM) uses thin optical slits for rapid scanning of the specimen. This allows for increased light output compared to SSCM and increases the speed at which an object can be scanned, as all points along the axis of the slit are scanned at the same time. Also the reflected light in the SSCM has greater intensity than the reflected light in a TSCM, so it requires a weaker illuminating source such as a 12V halogen lamp. One disadvantage is that the SSCM is truly confocal in only one axis. Clinical SSCMs are commercially available. The lateral resolution (x-y axis) has been reported as 0.8–1.4 μm, and the axial resolution (z axis) has been reported as 8–25 μm using the SSCM (Jalbert et al. 2003; Guthoff et al. 2009).

Laser Scanning Confocal Microscope

The laser scanning confocal microscope (LSCM) uses the basic configuration of a confocal microscope with a specific wavelength laser as the light source. Two oscillating mirrors are placed in the path of the beam of light in order to scan the specimen. LSCM can be used to view the anterior segment of the eye in vivo by placing a high-quality lens between the eye and the device, creating a laser focus less than 1 μm in diameter. This resolution provides the highest quality image and highest speed investigation of all layers of the cornea. LSCMs are commercially available. The

LSCM uses a single-wavelength laser, such as a 670 nm red laser, as its illumination source. This single-wavelength, coherent light source is less noisy than the nonuniform white light used in TSCM and SSCM, allowing for improved resolution, especially in the z axis. The lateral resolution (x-y axis) has been reported as approximately 2.0 μm, and the axial resolution (z axis) has been reported as approximately 4 μm using LSCM (Guthoff et al. 2006).

Contact Versus Noncontact In Vivo Scanning Confocal Microscopy

Contact in vivo scanning confocal microscopy is most frequently used to view the five layers of the cornea: the corneal epithelium, Bowman's layer, corneal stroma, Descemet's membrane, and corneal endothelium. In contact IV SCM, the objective tips of the TSCM and SSCM are optically coupled to the patient's cornea using a viscous gel. The LSCM uses a lens cap that forms a planar contact surface with the cornea using a coupling gel during contact IV SCM. The lens cap is able to keep the distance from the cornea to the microscope stable. Noncontact IV SCM can be used to image the tear film as well as the keratinocytes and endothelium of the cornea. Dynamic processes, such as breakup of tear film, can be viewed with noncontact LSCM due to its rapid imaging capabilities. For noncontact IV SCM, dry objectives are used with all three types of IV SCMs, and the lens cap of the LSCM is removed (Guthoff et al. 2006).

Indication

The full potential of in vivo scanning confocal microscopy has yet to be reached, and at this time it is commonly used for diagnosing infectious keratitis and for counting corneal nerves. The high resolution allows for in vivo visualization of fungal hyphae in keratomycosis and double-walled cysts in acanthamoeba keratitis. IV SCM has also been helpful when diagnosing Lyme borreliosis and herpetic and Thygeson's keratitis. Research is currently being done to explore possible future indications of IV SCM. Clinicians have successfully used it to diagnose other corneal diseases such as neurotrophic and toxic keratoconjunctivitis and characterize corneal dystrophies such as epithelial basement membrane and Reis-Bücklers', Meesmann's, lattice, fleck, granular, Schnyder crystalline, posterior polymorphous, and Fuchs dystrophies. Research has been done using IV SCM to study corneal wound healing after refractive surgeries and penetrating keratoplasties and also to study the effects of contact lenses on the cornea (Guthoff et al. 2009). More recently, IV SCM has been used to study both benign and malignant epithelial lesions of the conjunctiva, showing a high sensitivity and specificity for diagnosing melanocytic tumors (Guthoff et al. 2006).

Contraindication

Because in vivo scanning confocal microscopy is not an invasive diagnostic technique, few contraindications exist. Contact in vivo scanning microscopy should not be performed on any patient with an open globe, as the pressure created by the contact can further damage an open-globe injury. Patients with corneal epithelial disease can obtain a corneal abrasion after contact IV SCM imaging. Topical anesthetics, fluorescein sodium, and other dyes are often used during in vivo confocal microscopy (Guthoff et al. 2006). Before using any of those products, the operator should check for possible contraindications such as drug hypersensitivities.

Advantage/Disadvantage

The scanning confocal microscope allows for noninvasive high-resolution real-time imaging of eye structures at the cellular level and is specifically useful for viewing the cornea. Advantages include the ability to diagnose vision-threatening diseases that cannot be differentiated by slit-lamp

biomicroscopy, such as acanthamoeba and fungal keratitis, and to clearly define borders of conjunctival tumors to make sure there are clear margins during excision.

While the small focal area of IV SCM creates high resolution and shows incredible detail, its small field of view causes several disadvantages. Minute involuntary eye movements due to pulse, respiration, and ocular microsaccades can cause blurring of the image. The confocal microscope image can also defocus in multiple planes – not only in the transverse axis (x and y axes) but also in depth (z axis) – making clean images difficult to attain depending on patient cooperation. This is especially true with non-contact IV SCM, as it is difficult to keep the distance from the cornea to the microscope constant when the objective is not coupled to the cornea. The small field of view also makes it incredibly difficult to return to the same area of the cornea multiple times for sequential analysis. For contact in vivo scanning confocal microscopy, the image quality degrades over time and can leave compression artifacts as the coupling gel on the eye runs thin (Guthoff et al. 2009). Functional imaging using fluorescence microscopy or immunohistochemistry with IV SCM is limited due to the limited availability of dyes that are safe to use in the living eye. Current studies are using fluorescein and rose bengal staining (Guthoff et al. 2006).

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Scanning Electron Microscopy

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Definition

A scanning electron microscope (SEM) uses an electron beam which scans the object to generate a magnified image of the object from the interactions of the electrons with the object surface.

Structure

The electron beam is generated by an electron source which is usually an electron gun with a heated tungsten filament that thermionically emits the electron beam. To prevent interactions of the electrons with air, the sample is placed in a high vacuum chamber. The images of the sample are shown on a cathode ray tube.

Function

The beam with energy of 0.5–40 keV is focused to a spot of 0.4–5.0 nm in size. It is deflected to scan the specimen in a raster fashion over a rectangular area of the specimen surface. The interaction of the electrons with the surface causes scattering of electrons and emission of electromagnetic radiation. These are detected and amplified and shown on the cathode ray tube where they form a rastered magnified image of the specimen.

The magnification of a scanning electron microscope ranges from about 10 times to 500,000 times. It is not a function of the power of the objective lens but of the ratio between the raster size on the object and the raster size on the display.

All samples to be imaged by SRE must be electrically conductive. Therefore, metallic samples require little preparation except cleaning and mounting in the microscope chamber. Nonconductive samples like plastic materials or biological specimens require ultrathin coating of the surface (sputtering) with a conductive material, usually gold.

Clinical Relevance

SEM has been used extensively to show the ultrastructure of tissues and organs in biology, anatomy, and pathology. It is also extremely useful in assessing the surface quality of surgical instruments or intraocular implants (Versura and Maltarello 1988).

Cross-References

▶ Intraocular Lens

References

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SCD

▶ Comma Sign, in Sickle Cell Hemoglobinopathies

Scheimpflug Imaging

▶ Computerized Corneal Topography

Schirmer Lacrimation Test

▶ Schirmer Tests

Schirmer Tests

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Synonyms

Schirmer lacrimation test; Schirmer's tear test

Definition

The Schirmer test is the most commonly used procedure to evaluate tear production. The Schirmer test examines tear production through placing a filter paper under the eyelid and determining the length that tears reach on the paper in a certain period of time (Kaštelan et al. 2013). Therefore, the longer the distance that the tears are measured on the filter paper signifies a greater amount of tear production (Cho and Yap 1993).

Purpose

The purpose of the Schirmer test is to evaluate insufficient tear production in patients, and it is an indirect test for lacrimal gland dysfunction (Asbell and Lemp 2006). The results of the Schirmer test can be used to provide evidence for the diagnosis of dry eye disease or Sjogren's disease. The criteria vary, but a result of less than 5 mm on the strip is considered abnormal (Asbell and Lemp 2006).

Principle

There are multiple versions of the Schirmer test described below:

Schirmer I Test

– Blotting paper strip 5 × 35 mm is placed in the inferior cul-de-sac at the junction between the middle and lateral thirds of the lower eyelid. Both eyes are tested at the same time. (Savini et al. 2008)

– The strip is kept in place for 5 min, while the patient either gently closes their eyes or blinks normally.
– The strip is removed and the millimeters of wetness are assessed.

Variations of Schirmer I test can include using topical anesthetic, placing the strip in slightly different locations along the lower lid margin, or having the patients close their eyes, while the strip is in place. The Schirmer I test measures both basal and reflex tearing.

Schirmer II Test

– A similar method to the Schirmer I test is used. However, the eye is anesthetized beforehand and a cotton tip applicator is used to irritate the nasal mucosa. The Schirmer II test is often performed if the Schirmer I test is abnormal. The Schirmer II test measures only reflex tearing (Savini et al. 2008).

One-Minute Schirmer Test (Savini et al. 2008)

A 1-min version of the Schirmer I test has been proposed to minimize discomfort and save time. The 1-min Schirmer test with anesthesia has been shown to correlate with the 5-min Schirmer I test with anesthesia.

Phenol Red Thread Test

In this test, a fine thread with phenol red dye is used instead of filter paper and is inserted into the conjunctival sac for 15 s (Savini et al. 2008). The pH of tears will turn the thread red, and then the wetness of the tears can be measured.

Indication

The Schirmer test is used to diagnose insufficient tear production and is part of the diagnostic workup of dry eye disease. Dry eye could be due to a variety of factors including age, climate changes, infections, prior eyelid surgery, Sjogren's syndrome, vitamin-A deficiency, etc. The Schirmer test can also be used to evaluate tolerance for contact lens use (Cho and Yap 1993).

Contraindication

There are no noted contraindications for the Schirmer tests.

Advantage/Disadvantage

Advantages (Cho and Yap 1993):

– Widely used
– Commercially available
– Easy to perform

Disadvantages (Cho and Yap 1993):

– Large discrepancies in repeatability of the Schirmer test.
  (a) Changes in light, temperature, and patient anxiety can change reflex tearing rates and modify results.
– Ocular discomfort from the filter paper.
– Potential injury to the cornea if the paper shifts out of place.
– The mean Schirmer test results in normal subjects can vary widely.

Cross-References

▶ Dry Eye
▶ Keratoconjunctivitis Sicca
▶ Tear Breakup Time

References

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Schirmer's Tear Test

▶ Schirmer Tests

Schlichting Dystrophy

▶ Posterior Polymorphous Corneal Dystrophy

Schnyder Crystalline Corneal Dystrophy

▶ Corneal Dystrophies

Schnyder Crystalline Corneal Dystrophy (SCCD)

▶ Schnyder Crystalline Dystrophy Syndrome

Schnyder Crystalline Dystrophy Sine Crystals

▶ Schnyder Crystalline Dystrophy Syndrome

Schnyder Crystalline Dystrophy Syndrome

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Synonyms

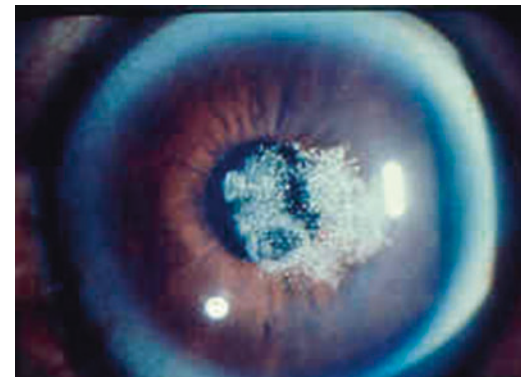
Central stromal crystalline corneal dystrophy; Crystalline stromal dystrophy; Hereditary crystalline stromal dystrophy of Schnyder; Schnyder crystalline corneal dystrophy (SCCD); Schnyder crystalline dystrophy sine crystals

Definition

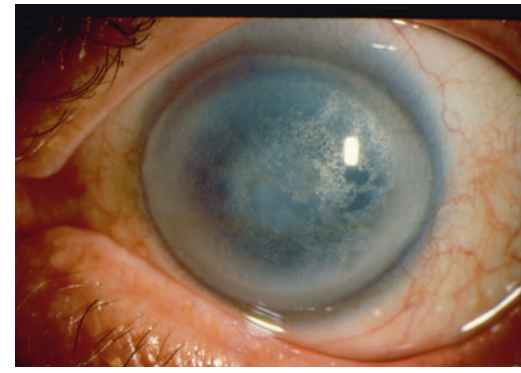
Schnyder corneal dystrophy is a progressive disease characterized by central corneal haze and crystals with lipid and cholesterol deposits in Bowman's layer and the anterior stroma (Figs. 1 and 2).

Etiology

Inheritance is autosomal dominant and there is an association with hypercholesterolemia and



Schnyder Crystalline Dystrophy Syndrome, Fig. 1 Central subepithelial crystalline deposition



Schnyder Crystalline Dystrophy Syndrome, Fig. 2 Advanced disease with crystalline deposits and arcus lipoides

genu valgum. The corneal deposits are possibly caused by a defect in cholesterol metabolism linked to a genetic mutation on chromosome 1 (Krachmer et al. 2011).

Clinical Presentation

Patients present in the second or third decade of life with central disciform corneal haze and polychromatic crystal deposits in Bowman's layer and the anterior stroma. Over the next decades, the haze becomes denser, the number of deposits increases, and presenile arcus lipoides develops. Eventually the entire cornea is hazy. Patients complain of glare and progressive vision deterioration. Decreased corneal sensation is found on examination (Weiss et al. 2008).

Diagnostics

Fasting blood level of cholesterol and lipoprotein electrophoresis can add in diagnosing hyperlipidemia. On histology, special stains such as oil red O and Sudan black highlight abnormal phospholipid and cholesterol deposits in the stroma, Bowman's layer, and basal epithelial cell layer. The crystals are birefringent. Sometimes the epithelial basement membrane is absent, and there is complete destruction of Bowman's layer from glycogen deposits. The stroma may reveal round empty spaces, signifying former fat deposits. Confocal microscopy demonstrates highly reflective intracellular and extracellular deposits (Weiss et al. 2008).

Differential Diagnosis

Differential diagnosis includes herpes simplex, acanthamoeba, Bietti's crystalline dystrophy, cystinosis, mucopolysaccharidoses, systemic disease with immunoglobulin deposition (lymphoma, benign monoclonal gammopathy, multiple myeloma, etc.), and haze from photorefractive keratectomy.

Prophylaxis

No prophylaxis is known.

Therapy

As the vision continues to decrease, superficial or phototherapeutic keratectomy may provide some benefit. However, keratoplasty, either lamellar or penetrating, is the treatment of choice when the vision has deteriorated significantly. The crystals frequently recur in the graft (Krachmer et al. 2011).

Prognosis

Progression is slow but most patients over 50 years old require keratoplasty for visual rehabilitation (Weiss et al. 2008).

Epidemiology

The disease is rare with the prevalence unknown.

Cross-References

- ▶ Bietti's Crystalline Dystrophy
- ▶ Cystinosis, Ocular Findings in, Retinal Degeneration
- ▶ Disciform Keratitis, Herpes Simplex Virus Causing
- ▶ Herpes Simplex Virus
- ▶ Mucopolysaccharidoses IV

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Schwalbe's Line

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Definition

The termination of Descemet's membrane located at the junction between the cornea and sclera which is located just anterior to the trabecular meshwork and identified by the corneal wedge when a thin slit beam is used during gonioscopy.

Cross-References

▶ Descemet's Membrane Endothelial Keratoplasty (DMEK)

Reference

Glaucoma: The Requisites

Scleral Buckle

▶ Encircling Buckle

Scleral Fixation of Intraocular Lens

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Synonyms

Transscleral fixation

Definition

Surgical technique for fixation of posterior chamber intraocular lenses (IOL) when capsular support is not effective. In contradiction to the surgical technique of iris fixation of posterior chamber lenses, scleral fixation is independent from the need of adequate iris tissue. Scleral fixation includes several different techniques as there are one-point, two-point, three-point, and four-point fixation. Some techniques for transscleral fixation include ab interno methods, in which the suture is passed from the inside of the eye to the external surface, and ab externo methods, in which the suture is initially passed from the external surface.

History

In 1986, two-site scleral fixation was first described by Malbran et al. Subsequently, in the following years, other techniques like one-site, three-site, and four-site fixation have been developed. Until today, there is a permanent employment and improvement of scleral fixation, for example, techniques with or without scleral flaps or techniques using suture retrieval through a scleral tunnel or sutureless intrascleral fixation of intraocular lenses which was first described by Maggi et al. in 1997. Sutureless scleral fixation was developed because disadvantages of suture scleral fixation were late exposure and breakage of sutures especially in patients with skin sclera or contraction following the use of diathermy.

Clinical Features

Generally posterior chamber intraocular lenses are implanted in the capsular bag of the crystalline lens. The capsular bag assures stability and adequate centration of the intraocular lens. In many cases, e.g., complicated cataract surgery, traumatic aphakia, or infantile eye deformities, the capsular of the crystalline lens can be damaged or absent. In these cases, other possibilities of

posterior chamber intraocular lens fixation are required such as scleral or iris fixation.

Tests

Postoperative checks for testing adequate intraocular position of the secondary intraocular lens should include best-uncorrected and best spectacle-corrected visual acuity, detailed slit-lamp examination in narrow and dilated pupil, and Scheimpflug imaging. Scleral suture should be controlled while slit-lamp examination.

Etiology

See "History" section above.

Treatment

As described in the history section, there exist many surgical techniques for secondary posterior chamber lens implantation by scleral fixation. In recent years, posterior chamber IOL implantation by means of intrascleral fixation without sutures has become more popular. The different surgical techniques are configured for different types of intraocular lenses and disbursed for different anatomical conditions. There exists, for example, a sutureless technique for sulcus fixation of a posterior chamber IOL using permanent incarceration of the haptics in a scleral tunnel parallel to the limbus which combines the control of a closed-eye system with the postoperative axial stability of the posterior chamber IOL. Other techniques are useful for situations in which adequate capsule and lens remain to support the second haptic. For more information please use current literature.

Cross-References

- ▶ Aphakic Spectacles
- ▶ Capsular Bag
- ▶ Intraocular Lens
- ▶ Iris-Fixated Phakic Intraocular Lens

References

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Scleral Laceration

▶ Corneoscleral Laceration

Scleral Patch Graft, Corneal Patch Graft

▶ Transplantation

Scleral Shell (To Be Used Only When It Covers an Eyeball Which May Be Blind, Unsightly, and/or Phthisical)

▶ Ocular Prostheses

Scleral Tunnel

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Synonyms

Sutureless scleral fixation

Definition

Surgical technique that is commonly used for sutureless fixation of posterior chamber intraocular lenses (IOLs) when capsular support is not effective. Scleral fixation can be performed under the protection of scleral flap. Techniques for transscleral fixation include ab interno methods, in which the suture is passed from inside of the eye to the external surface, and ab externo methods, in which the suture is initially passed from the external surface. Common to all the techniques is the necessity to bury, cover, or rotate the knot created for fixation so conjunctival erosion and endophthalmitis are less likely to develop. A variation of scleral flap technique is a nonperforating scleral tunnel which covers the knot created for scleral fixation.

Epidemiology

A scleral tunnel with hook retrieval of the suture ends can be used in any procedure requiring transscleral fixation including implantation of secondary IOL repair of dislocated IOLs, employment of adjunctive surgical devices such as Ahmed capsular tension segments and Cionni capsular tension rings, and repair of iridodialysis.

History

In 2006 Hoffmann et al. described the surgical technique of creating a scleral tunnel as a variation of posterior chamber intraocular lens fixation through transscleral fixation.

Clinical Features

Options for secondary intraocular lens implantation in an eye without capsular support include iris fixation and transscleral fixation through the ciliary sulcus or pars plana. Methods for scleral fixation of posterior chamber intraocular lenses are transscleral fixation or sutureless fixation through a scleral tunnel. The advantage of scleral tunnel fixation is that the construction of a scleral tunnel is easier than that of a triangular flap. Furthermore it affords a greater surface area for suture placement through ab externo or ab interno approach. The avoidance of rotation and cover of knots reduce the risk of complications such as conjunctival erosion or endophthalmitis.

Tests

Postoperative examinations for testing adequate intraocular position of the secondary intraocular lens should include best-uncorrected and best spectacle-corrected visual acuity, detailed slit-lamp examination in both narrow and dilated pupil, and Scheimpflug imaging.

Differential Diagnosis

Transscleral lens fixation.

Etiology

There are no datas available in this topic.

Treatment

In this technique a double-armed suture is passed through the roof of the scleral tunnel into the eye using an ab externo or ab interno approach. Retrieval of the suture ends through the external incision, and subsequently tying the knot allows the suture knot to pass under the roof of the tunnel, without the need for suture knot rotation.

Cross-References

▶ Endophthalmitis
▶ Sutureless Scleral Fixation

References

Hoffmann RS et al (2006) Scleral fixation using suture retrieval through a scleral tunnel. J Cataract Refract Surg 32:1259–1263

Scleritis

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Definition

Scleritis is inflammation of the sclera that is generally immune mediated but can infrequently be of infectious etiology. There is an association with systemic autoimmune diseases, notably rheumatoid arthritis (RA) and Wegener granulomatosis (WG). Immune-mediated scleritis is classified as anterior or posterior, with respect to the insertion of the extraocular rectus muscles. Anterior scleritis can be further subdivided into diffuse (the most common form), nodular, necrotizing, and necrotizing without inflammation (sclero-malacia perforans).

Etiology

It is believed that an underlying disordered immune response results in tissue and blood vessel damage characteristic of scleritis. Damage is mediated by immune complex deposition within the episcleral and scleral perforating capillary and postcapillary venules and a subsequent chronic granulomatous response. Inflammatory cells (macrophages, T cells, and B cells) and mediators (tumor necrosis factor-α, interleukin-1, interleukin-2, interleukin-3, interleukin-6, interferon-γ, and matrix metalloproteinases) are elevated in the sclera and overlying conjunctiva in patients with scleritis. Previous viral infection or self-antigens to connective tissue within the sclera can also instigate an autoimmune response (Krachmer et al. 2011).

Immune-mediated scleritis is most commonly caused by systemic autoimmune diseases (i.e., connective tissue disease, vasculitis), which about half of patients with scleritis have prior to presentation. The most commonly associated diseases in descending order are RA, WG, and relapsing polychondritis (Krachmer et al. 2011). The more severe necrotizing forms of anterior scleritis have a particularly high association with systemic disease. It is important to realize that scleritis may be the first sign of an underlying vasculitis or connective tissue disease.

Infectious scleritis is rare (4–18% of cases in a tertiary-care setting). Exogenous infections are the most common and can be posttraumatic and postsurgical or spread from surrounding ocular infection (i.e., keratitis, choroiditis, endophthalmitis). Endogenous infections are associated with systemic infections and can often present like immune-mediated scleritis. Tuberculosis, syphilis, leprosy, and Lyme disease are included in this category.

Clinical Presentation

Patients with scleritis present with pain worse with eye movement that characteristically radiates to the forehead, eyebrow, or jaw and may awaken the patient at night. The pain can be exquisitely tender. Other symptoms include tearing, photophobia, and blurry vision. The most common sign of scleritis is a violet-blue scleral hue with edema. In about half of patients, the presentation is bilateral. Non-ocular signs in conjunction with systemic disease may be present as well. Each form of scleritis has typical manifestations.

Anterior Scleritis

- Diffuse – In the most common and least severe form of scleritis, onset is gradual, starting with ocular redness and progressing to pain over a

couple of days, including the face and temple. The sclera may be salmon, violet, or blue underneath inflamed episclera. Vascular congestion and dilatation with edema is present. As the inflammation resolves, the sclera appears translucent or gray-blue as a result of rearrangement of scleral fibers.

- Nodular – Patients present with gradual ocular pain, increasing redness and tenderness, and the development of one or more scleral nodules. The nodules are yellow-red, firm, tender, immobile, and frequently found in the interpalpebral zone adjacent to the limbus. The sclera becomes more translucent with resolution.
- Necrotizing – The most aggressive and visually compromising form presents with gradual onset of severe pain radiating to the temple, brow, or jaw that may awaken the patient from sleep. On examination, necrosis appears as a dark area surrounded by active inflammation. White, avascular areas of the sclera develop with adjacent swelling and congestion. As the sclera thins, uveal tissue can be seen underneath the conjunctiva.
- Necrotizing without inflammation – This form is typically seen in older women with RA. Patients are often asymptomatic but may have non-specific irritation. There are avascular necrotic scleral plaques adjacent to the limbus with thinning of the sclera and episclera and uveal exposure.

Posterior Scleritis

Patients present with decreased vision, diplopia, and pain. Signs include chemosis, proptosis, periorbital edema, and ophthalmoplegia. Posterior segment findings include choroidal folds, uveal effusion, exudative retinal detachment, subretinal mass, and disk edema. There can be concomitant anterior scleritis.

Infectious Scleritis

The presentation can be similar to immune-mediated scleritis. Patients may complain of pain and irritation. Clinical signs include conjunctival or episcleral hyperemia, mucopurulent discharge, scleral necrosis, subconjunctival nodule, subconjunctival abscess, subconjunctival hemorrhage, uveitis, uveal prolapse, scleral perforation, and conjunctival ulceration. Infection spreading from the peripheral cornea may manifest as limbal erythema, edema, and infiltrate.

Diagnosis

A proper scleral examination is essential for diagnosis. On slit-lamp examination, congestion can be seen most prominently in the deep scleral vessels, which cannot be moved with a cotton-tipped applicator. Edema of the sclera can also be visualized. Red-free light enhances the blood vessels, particularly areas of nonperfusion. Topical administration of a sympathomimetic dilating drop (2.5–10% phenylephrine) blanches the superficial but not the deep vessels.

If suspicious for a systemic disorder, laboratory tests should be ordered. Non-specific markers of inflammation include increased erythrocyte sedimentation rate or C-reactive protein, anemia, leukocytosis, decreased complement, and circulating immune complexes. Screening for autoimmune disease includes antinuclear antibodies, rheumatoid factor, anti-DNA antibodies, anti-neutrophil cytoplasmic antibodies, anti-phospholipid antibodies, and HLA-B27.

Imaging can further assist with the diagnosis. Chest X-ray is useful in diagnosing WG, sarcoidosis, and Churg-Strauss syndrome. Joint X-rays can demonstrate arthritis. Fluorescein angiography (FA) detects areas of vascular nonperfusion seen in necrotizing scleritis. Additionally, patients with WG can have neovascularization, transudation, and localized vasculitis on FA. In posterior scleritis, B-scan ultrasound is used to assess for scleral thickening, scleral nodules, sub-Tenon fluid, disk edema, choroidal folds, or retinal detachment. MRI and CT can show scleral thickening and proptosis. Scleral biopsy is not typically performed but can determine if there is systemic inflammation, vasculitis, or infection.

Infectious scleritis is often diagnosed by culturing infected tissues, typically from the cornea or vitreous. Blood cultures and serologies can also be drawn.

Differential Diagnosis

Episcleritis is benign inflammation of the more superficial episclera that causes mild discomfort and has a red-colored appearance. In contrast, scleritis presents with more severe, radiating pain, and globe tenderness, with a deeper violet-blue hue. Topical administration of phenylephrine blanches the superficial blood vessels affected in episcleritis but not the deeper vessels inflamed in scleritis.

The differential for posterior scleritis includes thyroid eye disease, orbital inflammatory disease, orbital cellulitis, orbital tumors, choroidal tumors, and central serous retinopathy.

Therapy

Immune-Mediated Scleritis

- Oral nonsteroidal anti-inflammatory drugs (NSAIDs): This is the first-line treatment for non-necrotizing scleritis to reduce inflammation and pain. One NSAID at a time should be tried and switched if not effective for the individual patient. Months or years of therapy may be required. Topical forms are usually not efficacious.
- Systemic corticosteroids: Corticosteroids are indicated for necrotizing scleritis and severe non-necrotizing scleritis unresponsive to oral NSAIDs. Prednisone is dosed starting at 1 mg/kg/day and tapered based on clinical response. Topical steroids are not commonly used.
- Immunosuppressive agents: This therapy is used when the disease is uncontrolled with corticosteroids or NSAIDs or as a steroid-sparing alternative for those requiring long-term therapy. Patients with RA can be treated with methotrexate (up to 20–25 mg/week). Patients with WG are given cyclophosphamide starting at 2.5 mg/kg/day. Other agents include azathioprine (starting dose of 2.5 mg/kg/day), mycophenolate mofetil (2–3 g/day), and cyclosporine (2.5–5.0 mg/kg/day).
- Biologic agents: Use of biologic agents may be considered in cases refractory to other treatments. Infliximab (5 mg/kg infusions every 2–8 weeks) and rituximab are promising new drugs.
- Periocular steroid injections: These are used for non-necrotizing and necrotizing.
- Surgery: Emergent repair of scleral perforation or scleral thinning at risk of rupture is required in necrotizing scleritis and scleromalacia perforans. Tectonic scleral and peripheral corneal patch grafting can be performed. Newer techniques include conjunctiva-Müller muscle pedicle flap and tarsoconjunctival pedicle flap (Krachmer et al. 2011).

Infectious Scleritis

- Appropriate antimicrobial therapy against the causative organism
- Topical or systemic steroids to reduce inflammation
- Removal of foreign bodies or associated materials contributing to the infection
- Surgical debridement of infected tissue can ameliorate antibiotic response, if indicated

Prognosis

Almost 60% of patients with scleritis develop an ocular complication, most commonly late in their course. Vision loss occurs in 16–37% of patients. Vision-threatening sequelae include keratitis, uveitis, and glaucoma. Keratitis presents in 14–37% of patients, with peripheral ulcerative keratitis being the most severe form. Uveitis manifests in over one-third of patients. Glaucoma occurs in about 13% of patients (Krachmer et al. 2011).

Overall prognosis is dependent on the severity or form of the scleritis. In the diffuse form, duration is an average of 6 years, with recurrences less frequent after the first 18 months and an overall good visual prognosis. Nodular scleritis has a comparable duration as the diffuse form. More than 10% of patients develop the necrotizing form, but this can be mitigated with early treatment. Necrotizing scleritis has the worst visual prognosis; up to 82% of patients have been found to lose vision (Krachmer et al. 2011). Inflammation may progress to affect the anterior globe and peripheral cornea if not treated. In the necrotizing form without inflammation, vision loss is not common, although areas of scleral thinning often do not heal. Posterior

scleritis is rare but severe and can lead to rapid blindness. In infectious scleritis, the prognosis is worse with bacterial keratoscleritis.

Prognosis of scleritis with systemic disease depends on the disease itself. Necrotizing scleritis in WG is severe and may cause permanent visual loss. In RA or relapsing polychondritis, severity is intermediate. In spondyloarthropathies or systemic lupus erythematosus, prognosis is good and self-limiting.

Epidemiology

Scleritis most commonly occurs in the fourth to sixth decades. In immune-mediated scleritis, women are more affected than men. There is no known racial predominance. There is a 25–50% chance that patients with scleritis have a systemic disease causing their condition. In terms of systemic disease, 14% of patients with relapsing polychondritis, 10% of those with WG or inflammatory bowel disease, and 6% of those with polyarteritis nodosa or RA develop scleritis (Krachmer et al. 2011).

Cross-References

- ▶ Chemosis
- ▶ Corneal Patching
- ▶ Corticosteroids, Use in Ophthalmology
- ▶ Endophthalmitis
- ▶ Episcleritis: Overview
- ▶ Hyperemia, Conjunctival
- ▶ Keratitis
- ▶ Nonsteroidal Anti-inflammatory Drugs (NSAIDs)
- ▶ Orbital Cellulitis
- ▶ Peripheral Keratitis
- ▶ Proptosis
- ▶ Retinal Detachment
- ▶ Sarcoidosis
- ▶ Secondary Open-Angle Glaucoma
- ▶ Syphilis: Overview
- ▶ Thyroid Eye Disease
- ▶ Ultrasound Pachymetry
- ▶ Wegener Granulomatosis

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Scleritis with Keratitis

▶ Sclerokeratitis

Scleritis-Associated Peripheral Keratopathy

▶ Keratolysis (Corneal Melting), Marginal, Systemic Immune-Mediated Disease

Sclerocornea

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Synonyms

Severe anterior segment dysgenesis

Definition

Sclerocornea is a rare congenital malformation disorder characterized by bilateral, asymmetric scleral tissue extending anteriorly to the cornea (Gerstenblith et al. 2012). It can occur as a primary anomaly but can also be associated with other ocular defects (Elliott et al. 1985). Scleralization can occur in the peripheral cornea or can take over the entire cornea (Elliott et al. 1985). If the peripheral cornea is affected, it is vascularized with arcades of superficial scleral vessels (Elliott et al. 1985). In total sclerocornea, the entire cornea can become opaque and vascularized (Elliott et al. 1985).

The disease is nonprogressive and non-inflammatory (Harissi-Dagher and Colby 2008).

Etiology

Sclerocornea is due to a congenital abnormality of the anterior segment of the eye and is extremely rare (Elliott et al. 1985). It is thought that half of the cases of the disease are due to a sporadic mutation and half are inherited (Harissi-Dagher and Colby 2008). Of the cases that are inherited, the autosomal dominant forms of the disease are milder than the autosomal recessive forms (Harissi-Dagher and Colby 2008). In sclerocornea, there is a disruption in neural crest migration during embryogenesis and corneal development which leads to this anterior segment dysgenesis (Elliott et al. 1985). It is thought that the mesenchymal tissue that normally forms the cornea stroma does not form clear cornea but rather forms tissue that resembles the sclera instead (Garg et al. 2011).

Clinical Presentation

Patients with sclerocornea disease will present at birth. The degree of vision loss is dependent on the amount of scleralization of the cornea (Harissi-Dagher and Colby 2008). If the scleralization is only peripheral and has a relatively flat center, vision can be relatively normal (Harissi-Dagher and Colby 2008). If the scleralization extends to more areas of the cornea, it can prevent development of normal vision, and measures should be taken soon after birth to prevent irreversible deprivation amblyopia (Harissi-Dagher and Colby 2008).

Diagnosis

Sclerocornea is suspected when corneal opacity is detected at birth and the opacity is not associated with interstitial keratitis, ulceration, or an inflammatory disease of the cornea (Harissi-Dagher and Colby 2008). Other causes of congenital corneal opacity must be eliminated in order to diagnose sclerocornea (Harissi-Dagher and Colby 2008). Ultrasound biomicroscopy can also be used to help with diagnosis (Garg et al. 2011). Histologically, patients with sclerocornea have thickened collagen fibers in the superficial stroma of the cornea compared to the posterior stroma, which is a pattern that is normally seen in the sclera (Garg et al. 2011).

Differential Diagnosis

The differential diagnosis includes:

- Congenital glaucoma
- Peters anomaly
- Congenital hereditary endothelial dystrophy

Prophylaxis

None indicated for sclerocornea disease.

Therapy

Treatment of sclerocornea is often complex and depends on the severity of the disease (Binenbaum et al. 2008). Patients have to be monitored and treated for amblyopia, glaucoma, and other ocular abnormalities that may arise (Binenbaum et al. 2008). Keratoplasty is often considered if there is central opacification, but allografts have been shown to have a high rate of rejection (Binenbaum et al. 2008).

Prognosis

If the disease is limited to the periphery, vision may not be severely affected (Harissi-Dagher and Colby 2008). Keratoplasty is often indicated in more severe disease, and the rate of surgical success has increased in the past few decades (Harissi-Dagher and Colby 2008). However, the success rate for the procedure is still lower than that with other congenital corneal abnormalities (Harissi-Dagher and Colby 2008). Even after surgery, there is a risk for development of other

ocular abnormalities such as coloboma, glaucoma, and shallow anterior chambers that could lead to reduced vision (Harissi-Dagher and Colby 2008).

Epidemiology

Sclerocornea is usually bilateral and affects males and females with equal incidence (Garg et al. 2011).

Cross-References

► Anterior Segment Dysgenesis

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Sclerokeratitis

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Synonyms

Scleritis with keratitis

Definition

Scleritis is inflammation of the sclera and may occur with or without keratitis (inflammation of the cornea).

Disease

Sclerokeratitis is inflammation of the sclera with associated corneal inflammation. Patients with sclerokeratitis present with ocular redness, pain, and decreased vision. Any portion of the sclera may be inflamed. Keratitis, which can occur in association with scleritis, typically presents with peripheral corneal infiltrates, corneal thinning, and neovascularization.

Scleritis can be classified as anterior/posterior, diffuse, nodular, or necrotizing. Anterior scleritis is the most common presentation, accounting for 80–85% of all scleritis cases (Larson and Sen 2012). Diffuse anterior scleritis is the most common form of scleritis overall, occurring in approximately 60% of patients. Nodular scleritis is the second most common form and accounts for approximately 20% of cases. Patients with nodular scleritis typically exhibit a tender, firm, and immobile focal thickening of the sclera, often near the limbus (Galor and Thorne 2007). Necrotizing scleritis is the most severe and destructive form of scleritis and is most often associated with sight-threatening sequelae (Okhravi et al. 2005; Galor and Thorne 2007). Necrotizing scleritis usually occurs in older patients and is more likely to be associated with an underlying systemic disease (50–80%), especially rheumatoid arthritis and granulomatosis with polyangiitis. Patients with necrotizing scleritis typically present with features of anterior scleritis and areas of white sclera, which results from capillary closure of the episcleral vessels leading to necrosis of the underlying sclera. Corneal melting is uncommon but more likely to occur in the presence of anterior or necrotizing scleritis (Jabs et al. 2000; Galor and Thorne 2007). Scleromalacia perforans is a rare and severe form of necrotizing scleritis that tends to be bilateral and is unique in that patients do not present with pain, redness, or edema (Okhravi

et al. 2005; Galor and Thorne 2007; Larson and Sen 2012). There is often loss of the episclera and episcleral vasculature with localized areas of infarcted tissue, which may lead to thinning so severe that the underlying choroid is exposed. Classically, scleromalacia perforans develops in elderly women with a history of long-standing rheumatoid arthritis. It is unusual for a case of scleritis to evolve from one type to another (Galor and Thorne 2007).

Sclerokeratitis can occur in any age group but usually occurs between the ages of 30 and 50. Women are affected approximately twice as often as men. No geographic or racial predilections have been identified. The prevalence of scleritis is estimated to be six cases per 100,000 persons among the general population but may be as high as 0.2–6.3% and 7% among rheumatoid arthritis and granulomatosis with polyangiitis patients, respectively, making these the most commonly associated noninfectious systemic diseases in the setting of scleritis (Galor and Thorne 2007). Additional noninfectious systemic disease associations include connective tissue disease (juvenile rheumatoid arthritis, reactive arthritis, systemic lupus erythematosus, relapsing polychondritis, polymyositis, inflammatory bowel disease, and spondyloarthropathy), vasculitides (polyarteritis nodosa, allergic angiitis of Churg-Strauss, Cogan syndrome, Takayasu disease, Behcet disease, giant cell arteritis, and sarcoidosis), neoplastic processes such as lymphoma and metastases and gout (Okhravi et al. 2005; Larson and Sen 2012).

Infectious sclerokeratitis can be caused by viral, parasitic, fungal, and bacterial etiologies. Infections are more likely to occur in tissue compromised by disease, surgery, or trauma. Patients with a history of pterygium surgery, topical antimetabolite therapy, and retinal detachment repair may be at increased risk for developing infectious sclerokeratitis. Overall, the two most common causes of infectious sclerokeratitis are herpes zoster and syphilis. Other reported viral causes include Epstein-Barr and Coxsackie B5. Reported bacterial causes include tuberculosis, *Pseudomonas*, *Staphylococcus*, *Streptococcus*, *Mycobacterium*, *Haemophilus*, *Borrelia*, *Corynebacterium*, *Serratia*, *Nocardia*, leprosy, and *Listeria monocytogenes*. Fungal causes of scleritis include *Aspergillus*, *Scedosporium prolificans*, and *Sporothrix schenckii*. Acanthamoeba in association with keratitis and toxoplasmosis have also been reported as amoebic and parasitic etiologies, respectively (Okhravi et al. 2005).

Surgically induced necrotizing sclerokeratitis (SINS) occurs most commonly after cataract surgery when a corneal limbal incision is used. Interestingly, 75% of patients who develop SINS have undergone two or more surgical procedures prior to disease onset, and most who undergo systemic work-up are later diagnosed with systemic autoimmune disease. Patients tend to present anywhere from 2 weeks to 9 months postoperatively. Surgically induced diffuse scleritis has been reported, but is less well recognized (Okhravi et al. 2005).

Basic Science (Section Omitted: Combined with Pathology Section)

Pharmacotherapy

The therapeutic approach to sclerokeratitis varies based on the underlying etiology. Treatment with appropriate antimicrobials should be initiated immediately if there is suspicion for an infectious etiology. Most cases involve modulation of the inflammatory process to relieve symptoms and minimize further ocular injury. Sclerokeratitis associated with systemic disease generally requires more aggressive immunosuppressive therapy, as does the presence of posterior or necrotizing scleritis. Non-necrotizing scleritis may respond to systemic nonsteroidal anti-inflammatory drugs (NSAIDs), which include nonselective cyclooxygenase inhibitors (e.g., flurbiprofen and indomethacin). The most prominent side effects of these medications are gastrointestinal irritation and bleeding. Corticosteroids are typically used for patients with severe disease and those that have failed to respond to NSAIDs. Systemic corticosteroids can be administered orally or intravenously at high doses acutely to rapidly induce disease remission if an infectious etiology is not suspected. Oral prednisone is often

started at 1 mg/kg/day (maximum dose of 60 mg/day) and may be tapered based on clinical response. Intravenous methylprednisolone is useful when rapid control of inflammation is necessary, particularly in the setting of impending sclerocorneal perforation. Alternatively, local corticosteroid therapy, either with subconjunctival injections or topical difluprednate ophthalmic emulsion 0.05%, is occasionally used for cases of non-necrotizing anterior scleritis, particularly when patients are unable to tolerate systemic therapy. Although rare, cases of scleral melt after subconjunctival steroid injections have been reported (Jabs 2012). Other potential side effects of corticosteroid therapy are wide ranging and dependent on route of administration, dosage, and duration. Immunosuppressive therapy is typically considered for severe or recurrent ocular disease, particularly when chronic corticosteroid therapy in excess of 7.5–10 mg/day of prednisone is required for control of inflammation. Immunosuppressive therapy is particularly appropriate in patients with sclerokeratitis and an underlying systemic disease associated with increased mortality (Okhravi et al. 2005; Larson and Sen 2012).

Non-pharmacotherapy

Surgical intervention for sclerokeratitis may be necessary in clinical situations that require biopsy of the episclera, superficial sclera, and/or cornea to exclude potential infectious and neoplastic etiologies. Elective or emergent tectonic repair may also be indicated to prevent or treat globe perforation. Corneal perforations are more common than full-thickness scleral defects and may require emergent repair with lamellar or penetrating keratoplasty. In some instances, small corneal perforations may be glued and/or covered with a contact lens as temporizing measure while the inflammatory process is treated, or a more definitive surgical intervention is planned. Ultimately, control of the inflammatory process is essential for graft survival. Donor sclera is more robust than donor corneal tissue, and several other tissues may be used for scleral tectonic grafts, including fascia lata, pericardium, and dura. Cataracts and glaucoma may develop as a result of sclerokeratitis and/or corticosteroid therapy, but elective surgical interventions should ideally be delayed until disease quiescence is established. Trabeculectomy may be especially challenging as a result of scleral thinning, thereby necessitating tube-shunt placement (Okhravi et al. 2005).

Diagnostic Procedures

Patients with sclerokeratitis may present in the absence of any known associated systemic disease. The physician may elect to pursue a medical work-up, based on the patient's past medical history and review of systems. A targeted and cost-efficient approach to testing should be emphasized. Work-up may include testing for granulomatosis with polyangiitis, which generally consists of a chest x-ray or chest CT, cytoplasmic antineutrophil cytoplasmic antibody (c-ANCA), and urinalysis with microscopy. Likewise, perinuclear antineutrophil cytoplasmic antibody (p-ANCA) may be ordered to assess for the possibility of polyarteritis nodosa and other vasculitides. Testing for rheumatoid arthritis (rheumatoid factor, anti-citrullinated cyclic protein) and systemic lupus erythematosus (antinuclear antibody, anti-dsDNA) may be ordered when clinically indicated. HLA-B27 testing and further work-up may be indicated for patients with findings or symptoms concerning for seronegative spondyloarthropathies or inflammatory bowel disease.

Serologic testing for syphilis includes treponemal-specific (fluorescent treponemal antibody absorption [FTA-Abs]) and nonspecific (rapid plasma regain [RPR] or venereal disease research laboratory [VDRL]) tests. When risk factors are present, evaluation for tuberculosis can be done with a purified protein derivative (PPD) skin test or interferon gamma release assay (QuantiFERON-TB Gold). Serologies for viral hepatitis and Lyme disease may be indicated. Orbital CT imaging may be considered in atypical cases. Cultures and/or corneoscleral biopsy may be necessary in cases of suspected infectious sclerokeratitis (Okhravi et al. 2005; Galor and Thorne 2007; Larson and Sen 2012).

Signs and Symptoms

Scleral inflammation may be unilateral or bilateral and typically produces prominent pain and redness, which may occur focally or diffusely. Vascular engorgement of the deep episcleral plexus produces a characteristic violaceous hue in sclerokeratitis, which is in contrast to the red hue produced by dilation of conjunctival vessels and superficial episcleral plexus that occurs in episcleritis. Examination performed in natural lighting can be very useful in making this discrimination, as these hue distinctions may be difficult to appreciate on slit lamp examination. Conjunctival and superficial episcleral vessels blanch with 2.5–10% phenylephrine and are mobile with a cotton-tipped applicator, while deeper vessels generally do not blanch and are not mobile. This is in contrast to the findings of episcleritis, in which the affected vessels are more superficial and, as a result, are noted to be freely mobile and responsive to topical phenylephrine (Okhravi et al. 2005; Larson and Sen 2012).

Interstitial keratitis, defined as stromal inflammation with an intact epithelium, may develop (Akpek et al. 2004). In these cases, examination may reveal stromal haze with or without the presence of active peripheral corneal neovascularization and associated intrastromal lipoprotein exudates. Peripheral ulcerative keratitis may also occur, with epithelial breakdown, corneal inflammation, and loss of stromal tissue. Rearrangement of scleral collagen fibers following diffuse anterior scleritis may result in the sclera taking on a blue-gray hue, which does not represent thinning. Alternatively, necrotizing scleritis can result in scleral thinning and translucency, which allows the underlying uveal tissue to be seen (Galor and Thorne 2007).

The characteristic symptom of sclerokeratitis is severe, "boring" pain in the eye and/or orbit, which may radiate to involve regions of the face. Patients with sclerokeratitis typically notice redness and tenderness of the globe and may experience associated tearing and photophobia. Sclerokeratitis generally has a subacute onset, worsening over the course of days to weeks. Pain is often exacerbated with eye movement, can limit the ability to perform normal daily activities, and may even awaken patients from sleep (Okhravi et al. 2005).

Major Studies and Classifications

In 2004, Akpek and colleagues reported a series of 243 patients with scleritis. Of these patients, 37% had an associated rheumatic disease, and an additional 7% had an underlying infectious cause. The most frequent infection was herpes zoster and the most frequent rheumatic disease was rheumatoid arthritis. Of the 107 patients with an underlying disease, 77.6% had a previously diagnosed disease, 14% were diagnosed as a result of their initial work-up, and 8.4% developed a systemic disease during follow-up. Keratitis was present in 18.2% of patients.

Pathology

Most eyes with sclerokeratitis are not biopsied or enucleated, and studies on the pathogenesis of scleritis are limited. Available data suggests that T cells play an important role in the inflammatory process. Evidence of vasculitis with fibrinoid necrosis and neutrophil invasion of the vessel wall, as well as antibody deposition, has been described. Plasma cells may also be involved through the production of metalloproteinases and TNF-alpha. However, additional studies displayed a lack of antibody or complement deposition, suggesting that T cells are the primary effector cell in scleritis (Okhravi et al. 2005; Galor and Thorne 2007).

Diagnosis and Treatment

The broad differential of sclerokeratitis includes episcleritis, conjunctivitis, blepharitis, keratoconjunctivitis sicca, anterior uveitis, acute angle closure glaucoma, carotid or dural sinus fistula, conjunctival mucosa-associated lymphoid tissue lymphoma, and sentinel vessels in the setting of uveal melanoma (Okhravi et al. 2005; Galor and Thorne 2007). The main goal of treatment in the

acute setting is rapid control of inflammation. The long-term goals of treatment are the prevention of recurrences, structural complications, and vision loss. Also of critical importance is the diagnosis and treatment of underlying systemic disease when present. Various treatment strategies may be employed based on the known or presumed underlying etiology and are discussed in the pharmacotherapy portion of this article.

Potential ocular complications associated with sclerokeratitis include scleral and corneal thinning/perforation, anterior segment ischemia, glaucoma, hypotony, uveitis, and cataract (Okhravi et al. 2005). Among patients with anterior or necrotizing scleritis, corneal complications were the most common ocular complications (Jabs et al. 2000). One study reported the incidence of cataract and glaucoma as 17% and 13%, respectively (Okhravi et al. 2005). In a retrospective chart review by Jabs and colleagues in 2000, ocular complications occurred in nearly 59% of patients with scleritis, while approximately 56% of patients with diffuse anterior scleritis and 21% of patients with nodular anterior scleritis were treated with oral corticosteroids or immunosuppressive drugs. In summary, disease prognosis varies widely based on the site of inflammation, type of scleritis, associated complications, the presence or absence of underlying systemic disease, response to therapy, and the risk of side effects resulting from treatment (Larson and Sen 2012).

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Scleromalacia: Overview

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Synonyms

Necrotizing scleritis without inflammation

Definition

An aggressive form of scleritis presenting with necrosis but no signs of inflammation.

Etiology

Unknown

Clinical Presentation

Patients with scleromalacia perforans present with deep scleral ulcerations. These scleral ulcerations coalesce, and the thinned sclera shows a bluish color from the underlying uveal tissue. There is a lack of pain, inflammation, or vascular congestion, which distinguishes this condition from the closely related necrotizing scleritis (McCormick and Aquavella 2008; Kanski and Bowling 2011). Examination reveals yellow necrotic lesions near the limbus (McCormick and Aquavella 2008; Kanski and Bowling 2011). These will slough off and leave defects in the sclera.

Diagnosis

No lab diagnostics

Differential Diagnosis

Episcleritis

Necrotizing Scleritis
Conjunctivitis
Scleral hyaline plaque

Prophylaxis

Unclear

Therapy

When complications arise or the disease progresses, treatment is indicated. Immunomodulatory drugs have been effective despite the lack of clinically observable inflammation. Topical prednisolone and prednisone have been shown effective when combined with phenylbutazone or cyclophosphamide (McCormick and Aquavella 2008). After the eye has stabilized, the steroids should be tapered over several weeks. NSAIDs do not help in treating the disease. Eye protection during active disease is important because of the high risk of perforation secondary to trauma (Virasch et al. 2011). If the medical therapies fail, surgical methods must be used to reinforce the thinned sclera or repair perforations. This can include scleral autografts or grafts using preserved sclera or a variety of other tissues (McCormick and Aquavella 2008).

Prognosis

Perforation is an unlikely event for scleromalacia perforans (McCormick and Aquavella 2008). However, even minor trauma carries a high risk of perforation.

Epidemiology

While scleromalacia perforans can present in anyone, it classically presents in postmenopausal women who have long histories of rheumatoid arthritis (Goldstein and Tessler 2009).

Cross-References

- ▶ Conjunctivitis
- ▶ Episcleritis: Overview
- ▶ Necrotizing Scleritis
- ▶ Scleritis

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S-Cone Monochromacy

▶ Blue Cone Monochromatism

Scoptopic Pupil Diameter

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Synonyms

Pupil diameter under low light conditions

Definition

Pupil size measured upon reduced illumination.

Purpose

To help estimate expectable postoperative visual symptoms such as glare and halos or photophobia prior to refractive surgery. In keratorefractive surgery, postoperative visual symptoms can be caused by disparity between scotopic pupil size and the effective optical zone. Complaints of patients having refractive lens surgery are associated with optical aberrations becoming more dominant when the pupil dilates (Kohnen and Kasper 2006).

Principle

Preoperative measurement of pupil size using a binocular pupillometer providing different lighting conditions.

Indication

Measurement of the scotopic pupil diameter is crucial in the preoperative evaluation of patients undergoing refractive surgery and is a key inclusion or exclusion criterion (Kohnen et al. 2004).

Advantage/Disadvantage

To help identify patients who are likely to experience visual symptoms such as glare and halo after refractive surgery.

Cross-References

- ▶ Dark Adaptation Testing
- ▶ Glare, General
- ▶ Photophobia
- ▶ Pupil Center
- ▶ Refractive Surgery

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Sealed Capsule Irrigation Device

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Synonyms

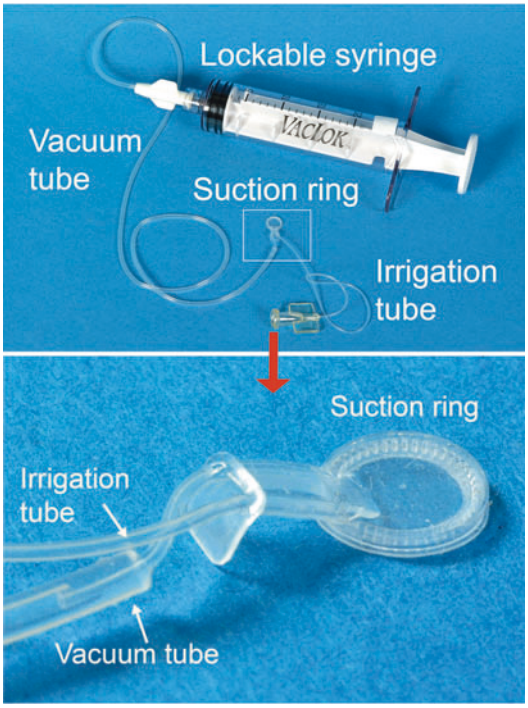
Perfect Capsule device

Definition

The sealed capsule irrigation device (Milvella Pty. Ltd., Sydney, Australia) allows selective targeting of lens epithelial cells by temporarily sealing the capsular bag. The device is made of silicone and consists of a foldable suction ring (overall diameter: 7.0 mm; inner diameter: 5.0 mm) and two separate lines (Fig. 1) (Rabsilber and Auffarth 2006).

History

The use of the device was first published in 2003 (Agarwal et al. 2003; Maloof et al. 2003). Compared to the first model, the system has been improved over time. A cogwheel pattern of the suction ring rim is supposed to provide an even stronger vacuum sealing. Furthermore, the irrigation process is facilitated by adding a second tube instead of the former channel.



Sealed Capsule Irrigation Device, Fig. 1 Perfect Capsule device for sealed capsule irrigation

Treatment

After cataract removal the device is inserted in the anterior chamber and positioned onto the anterior capsule covering the capsulorhexis completely. One tube is now used for vacuum application via the lockable syringe and the second one for irrigation of the internal capsular bag using pharmacological agents. The procedure is also known as sealed capsule irrigation (SCI).

Clinical Features

The device has been investigated in experimental as well as in clinical studies (Abdelwahab et al. 2006; Rabsilber et al. 2007). No complications occurred once the vacuum was built up and corneal endothelial cell count as well as pachymetry was stable postoperatively. The sealed capsule irrigation procedure was not feasible in eyes with deep anterior chambers, small pupils, or capsulorhexis diameters larger than five mm. Using distilled water, no statistically significant difference was found in terms of posterior capsule opacification prevention comparing treated eyes with corresponding control eyes two years after surgery (Rabsilber et al. 2007). Similar results were found in young rabbit eyes with highly proliferative cells. The vacuum to the anterior capsule was tight, and the system was sealed in all eyes. Distilled deionized water did not prevent capsular bag opacification but 5-fluorouracil reduced after cataract significantly (Abdelwahab et al. 2006).

In summary, it has been shown that the sealed capsule irrigation device and procedure are safe without causing any damage to surrounding tissues and effective in the experimental setup with regard to cytotoxic substances; however, it has not become a routine clinical treatment yet. Further developments have to be awaited.

Cross-References

- ▶ Capsular Bag Opacification
- ▶ Lens Epithelial Cells
- ▶ Posterior Capsule Opacification (PCO)

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Seasonal Allergic Conjunctivitis

► Allergic Conjunctivitis

Sebaceous Adenoma

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Definition

A benign tumor that is derived from sebaceous glands.

Etiology

Sebaceous adenoma is a rare benign tumor. Some are associated with Muir-Torre syndrome (autosomal dominant disease) (Albert and Jakobiec 2008; Shields and Shields 2008).

Clinical Presentation

It typically presents as a solitary, small, yellow papula or nodule which has a predilection for the face (particularly the eyelids) or for the scalp. It may be solitary or when numerous be associated with the Muir-Torre syndrome. Patients with the Muir-Torre syndrome develop multiple cutaneous sebaceous neoplasms and occasionally keratoacanthomas, as well as multiple adenocarcinomas of the colon, stomach, and duodenum (Albert and Jakobiec 2008; Shields and Shields 2008).

Diagnostics

Biopsy of this lesion with histopathology analysis.

Differential Diagnosis

Differential diagnosis includes apocrine hidradenoma, dermoid cyst, sebaceous hyperplasia, basal cell carcinoma, and sebaceous carcinoma.

Prophylaxis

Unknown.

Therapy

Solitary lesions are treated by complete surgical removal.

Prognosis

Good. Incomplete removal has occasionally resulted in local recurrence.

Epidemiology

Sebaceous adenoma is the most common benign neoplasm of the sebaceous glands.

Cross-References

► Basal Cell Carcinoma of Eyelid
► Epidermoid Cysts
► Hidrocystoma, Apocrine
► Sebaceous Carcinoma

References

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Sebaceous Carcinoma

► Sebaceous Glands of Eyelid, Tumors Arising in

Sebaceous Carcinoma of the Eyelid

► Sebaceous Gland Carcinoma: Overview

Sebaceous Carcinoma/ Adenocarcinoma

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Synonyms

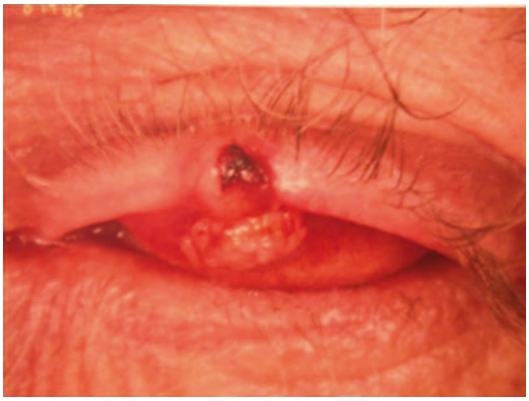
Meibomian gland carcinoma; Sebaceous cell carcinoma; Sebaceous gland carcinoma

Definition

Sebaceous carcinoma (SC) is an aggressive malignant neoplasm arising in the holocrine adnexal epithelium of sebaceous glands.

Etiology

The most common site of origin is the meibomian glands of tarsal plate. However, this neoplasm can occur in other sebaceous glands, such as in the caruncle, the glands of Zeis, and in the eyebrow. SCs are typically found in women, more often in the seventh decade of life, and they usually are on the upper eyelid margin since here are more meibomian glands in the upper lid than the lower lid (Fig. 1). Although sebaceous cell carcinomas are more common in elderly patients, they may be seen in younger patients with a history of radiation to the face, immunosuppressed, and can be associated with the Muir-Torre Syndrome (Shields et al. 2005; Albert and Jakobiec 2008; Shields and Shields 2008).



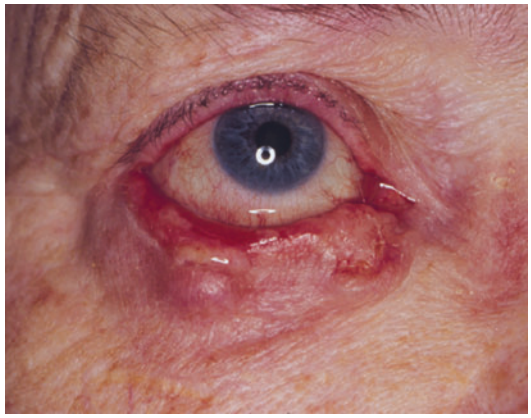
Sebaceous Carcinoma/Adenocarcinoma, Fig. 1 Sebaceous carcinoma presenting on the superior tarsal conjunctiva, seen with eyelid everted

Clinical Presentation

Highly variable. Classically, this lesion is a firm, painless nodule associated with the loss of cilia that in early stages is often misdiagnosed as a chalazion. The diffuse growth pattern presents as diffuse tarsal thickening that can mimic unilateral blepharoconjunctivitis (Fig. 2). Diffuse intraepithelial spread can extend in a pagetoid pattern across the tarsal and bulbar conjunctiva.

Diagnostics

Biopsy should be considered for recurrent chalazion or unilateral blepharitis resistant to usual treatment. Biopsy usually requires a full thickness lid section sent for histopathologic evaluation. Either fresh tissue or formalin-fixed tissue not exposed to alcohol can be frozen. Conjunctival map biopsies are very important in determining the extent of the lesion and detecting pagetoid



Sebaceous Carcinoma/Adenocarcinoma, Fig. 2 Sebaceous carcinoma on the lower eyelid mimicking unilateral blepharoconjunctivitis

spread (Shields et al. 2005; Albert and Jakobiec 2008; Shields and Shields 2008).

Differential Diagnosis

Differential diagnosis includes ▶ chalazion, ▶ blepharoconjunctivitis/keratoconjunctivitis, ▶ basal cell carcinoma ▶ squamous cell carcinoma, ▶ melanoma, Merkel cell carcinoma, and ▶ sweat gland neoplasms.

Prophylaxis

Unclear

Therapy

Wide surgical excision with frozen section or Mohs micrographic surgery is standard treatment for primary SC. Lymph node evaluation is necessary to evaluate metastasis. Treatment for pagetoid spread controversial (options include cryotherapy, topical mitomycin C, or exenteration when associated with anterior orbital tissue invasion). For metastatic disease, radiation and/or chemotherapy may be applicable (Shields et al. 2005; Albert and Jakobiec 2008; Shields and Shields 2008).

Prognosis

SC is characterized for masquerading as benign or malignant lesions, resulting in delays in diagnosis and relatively high morbidity and mortality. It invades locally and can metastasize to regional lymph nodes and distant organs. The sites of metastasis include lungs, liver, and bone. Mortality increases with increasing tumor size (diameter exceeding 10 mm) (Shields et al. 2005; Albert and Jakobiec 2008; Shields and Shields 2008).

Epidemiology

5–7% of malignant eyelid tumors.

Cross-References

- ▶ Basal Cell Carcinoma of Eyelid
- ▶ Blepharoconjunctivitis
- ▶ Chalazion
- ▶ Keratoconjunctivitis: Overview
- ▶ Melanoma of the Eyelid
- ▶ Squamous Cell Carcinoma of Eyelid
- ▶ Sweat Glands of Eyelid

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Sebaceous Cell Carcinoma

- ▶ Sebaceous Carcinoma/Adenocarcinoma
- ▶ Sebaceous Gland Carcinoma: Overview

Sebaceous Cyst

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Synonyms

Pilar cyst; Trichilemmal cyst

Definition

A fluid cavity secondary to obstruction of the duct of a sebaceous gland.

Etiology

Occlusion of meibomian glands, Zeis gland, or sebaceous gland associated with hair follicles of the lid or brow region (Albert and Jakobiec 2008; Shields and Shields 2008).

Clinical Presentation

Sebaceous cyst can be solitary or multiple and appear as smooth, elevated, yellow subcutaneous lesions. It may have a waxy comedo plug in the center and is filled with epithelial cells, keratin, fats and cholesterol crystals. Calcification may be seen.

Diagnostics

Biopsy and histopathological examination. May be clinically indistinguishable from epidermal inclusion cysts.

Differential Diagnosis

Differential diagnosis includes ▶ fibroma, ▶ epidermal inclusion cyst, and ▶ xanthelasma.

Prophylaxis

Unknown

Therapy

Observation or surgical excision with removal of the cyst capsule.

Prognosis

Excellent

Epidemiology

Most lesions are found on the scalp (90%) and less common on the brow region and medial canthus of the eyelid (Albert and Jakobiec 2008; Shields and Shields 2008).

Cross-References

- ▶ Epidermal Cysts, of the Eyelid
- ▶ Epidermal Inclusion Cyst
- ▶ Xanthelasma

References

Albert D, Jakobiec F (2008) Principles and practice of ophthalmology, 3rd edn. Saunders, Philadelphia, pp 3245–3246
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Sebaceous Gland Adenoma

▶ Sebaceous Glands of Eyelid, Tumors Arising in

Sebaceous Gland Carcinoma

▶ Sebaceous Carcinoma/Adenocarcinoma

Sebaceous Gland Carcinoma: Overview

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Synonyms

Sebaceous carcinoma of the eyelid; Sebaceous cell carcinoma

Definition

Rare, aggressive, malignant neoplasm arising from sebaceous glands of the skin adnexa.

Epidemiology

In the United States, SGC is the fourth most common eyelid tumor after basal cell carcinoma, squamous cell carcinoma, and melanoma, and it represents approximately 5% (2–7%) of eyelid malignancies. In Asian countries like India and China, where basal cell carcinoma is less common, SGC represents about a third to a half of all malignant eyelid neoplasms.

SGC typically occurs in the sixth or seventh decade of life, with a wide age range from early childhood through the 90s. There is a predilection for women – more than one half up to three-fourths of cases occurs in women without any clear explanation for the preponderance (Niederhuber et al. 2013; Shields and Shields 2008).

Etiology

The etiology is not entirely known. Though sebaceous gland carcinoma (SGC) is more common in elderly patients, it has been reported in patients who have undergone radiation therapy for hemangioma, facial acne, or eczema at any age or hereditary retinoblastoma patients who received external beam radiotherapy in their teenage years. There also appears to be a greater preponderance of SGC and Merkel cell carcinoma in younger age groups of immunocompromised patients with acquired immunodeficiency syndrome (AIDS) and organ transplantation (Niederhuber et al. 2013; Shields and Shields 2008).

Clinical Presentation

SGC presents as a solitary, tarsal nodule in approximately 40% of cases and as a diffuse thickening of the eyelids in about 60% of cases. In the solitary form, the firm tarsal nodule becomes yellow and causes overlying loss of cilia as it grows. Ulceration is uncommon but may occur in advanced cases. In the early stages, this form is frequently misdiagnosed as a chalazion. The diffuse growth pattern is responsible for SGC masquerading as chronic blepharoconjunctivitis. Other less common presentations include eyelid margin lesion from Zeis gland involvement, lacrimal gland mass from deeper invasion of subtle or subclinical eyelid lesion, pedunculated mass, and yellow enlargement of caruncle (Niederhuber et al. 2013; Shields and Shields 2008).

Approximately two-thirds of sebaceous carcinomas arise in the upper eyelid, reflecting the greater mass of meibomian gland tissue in the upper eyelid as compared to the lower eyelid. Though the meibomian gland is the most common site of origin, SGC may also arise from sebaceous glands of the cilia (Zeis glands), caruncle, or eyebrow (Niederhuber et al. 2013).

SGC may exhibit locally aggressive behavior and metastasize to regional lymph nodes and distant organs. SGC may spread by direct or perineural extension into the orbit, sinuses, and intracranially (Niederhuber et al. 2013; Shields and Shields 2008). SGC metastasizes via hematolymphoid channels to preauricular and cervical lymph nodes, the lungs, liver, brain, and

skull. The lung and the liver are the most common sites of distant metastasis (Patterson 2013).

SGC, like sebaceous adenoma, may be associated with Muir-Torre syndrome, an autosomal dominant, inherited syndrome caused by defects in mismatch repair genes, which predispose patients to gastrointestinal and genitourinary tract malignancies. Almost half of patients with SGC have been reported to have additional visceral neoplasms (Niederhuber et al. 2013; Shields and Shields 2008; Patterson 2013).

Diagnosis

The mean duration of signs or symptoms before diagnosis is 2 years. Historically, SGC has been notorious for masquerading as other benign and malignant lesions. Although ophthalmologists are more familiar with the clinical variability of periorbital SGC, there remain delays in diagnosis and misdirected therapy, which translate into increased morbidity and mortality. Given the aggressive, potentially lethal nature of SGC and variability of presentation, one must have a high index of suspicion and low threshold for biopsy. Any elderly patient with chronic, unilateral blepharoconjunctivitis or keratoconjunctivitis that does not respond to treatment should have a biopsy. Chronic and/or recurrent chalazia in the right clinical context should also be submitted for histopathologic examination.

Clinically, there are no pathognomonic features of SGC that differentiate it from other epidermal lesions. In contrast to most cases of blepharitis, SGC is unilateral and tends to cause more thickening and induration. In contrast to the typical chalazion, SGC tends to cause madarosis and destruction of meibomian gland orifices.

In patients who present with a chronic inflammatory condition, SGC frequently exhibits pagetoid spread or conjunctival intraepithelial invasion. In those with diffuse conjunctival involvement, the superior tarsus, conjunctiva, and fornix are involved in almost all cases. Direct orbital invasion occurs in about 10–15% of cases (Niederhuber et al. 2013; Shields and Shields 2008).

Pathology

Microscopically, sebaceous carcinoma is defined by cells with a characteristic lipid-rich and vacuolated cytoplasm. This is not to be confused with the cytoplasmic clearing seen in clear cell carcinomas, either primary in the skin or metastatic (e.g., metastatic clear cell renal cell carcinoma). Lipid stains such as Oil Red O or Sudan IV can be used to help confirm intracytoplasmic lipid but must be done on frozen section, as solvents used in standard tissue processing and paraffin embedding dissolve fat. Although there are several methods of classifying SGC, there are four recognized histopathologic patterns: lobular, comedocarcinoma (central necrosis), papillary, and mixed (any combination of the three patterns). It may be further grouped into well-, moderately, and poorly differentiated varieties. By immunohistochemistry, sebaceous carcinomas are immunopositive to epithelial membrane antigen (EMA), Ber-EP4, and others including cytokeratin 7, Cam5.2, and BRST-1. EMA is typically negative in basal cell carcinoma, and Ber-EP4 is typically negative in squamous cell carcinoma; this profile can be helpful when attempting to determine if a poorly differentiated tumor is of sebaceous, squamous, or basal cell origin. P16 readily highlights pagetoid cells within the epidermis and conjunctival epithelium (Niederhuber et al. 2013; Patterson 2013; Cummings 2012; Eagle 2011).

Differential Diagnosis

SGC must be differentiated from other malignant neoplasms such as basal cell carcinoma, squamous cell carcinoma, and Merkel cell carcinoma and from inflammatory conditions like chalazion and blepharoconjunctivitis (Niederhuber et al. 2013).

Prophylaxis

No clear method of prophylaxis exists. However, limiting or avoiding ionization radiation where possible may lower risk of developing SGC.

Therapy

Treatment must be tailored to the patient based on extent of disease and specific needs of the patient. In cases with diffuse conjunctival involvement, multiple mapping biopsy specimens should be obtained and submitted for histopathologic examination to guide surgical planning. The mainstay of treatment for SGC without orbital involvement is wide, local excision with monitoring of margins with both permanent and frozen sections. In the majority (~75%) of cases, initial management is surgical excision with or without cryotherapy. In cases with extension beyond the basement membrane and orbital involvement, exenteration is often warranted. In the 5–10% of cases with perineural invasion, there may be a role for postoperative adjuvant radiotherapy after primary excision. External beam radiotherapy (EBRT) is reported to be a safe, effective, curative treatment for eyelid SGC when a dose of greater than 55 Gy is used. In the appropriate setting, brachytherapy with ^{192}Ir or similar isotopes should be considered as an alternative to surgical excision. Complications of surgical procedures, cryotherapy, and radiation of the eyelids and conjunctiva include eyelid and conjunctival scarring, symblepharon, and eyelid malpositioning. Finally, there is a role for antimetabolites such as mitomycin C in treating superficial SGC with diffuse intraepithelial involvement (Niederhuber et al. 2013; Shields and Shields 2008).

Prognosis

Although SGC is a highly malignant neoplasm, the prognosis is improving, as clinicians and pathologists become more familiar with the condition, leading to earlier recognition and more efficient treatment (Shields and Shields 2008). Tumor mortality is estimated to about 15%. Factors associated with poor prognosis include upper eyelid origin, meibomian gland origin, diameter >10 mm, duration of symptoms before diagnosis >6 months, infiltrative growth pattern, poor sebaceous differentiation, extensive pagetoid invasion, and invasion of lymphatics, vessels, and the orbit (Eagle 2011). With wide excision and no evidence of metastasis, surgery results in cure. However, sebaceous lesions have a high incidence of recurrence and metastasis.

Cross-References

- ▶ Blepharoconjunctivitis
- ▶ Chalazion

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Sebaceous Gland Hyperplasia

- ▶ Sebaceous Glands of Eyelid, Tumors Arising in
- ▶ Sebaceous Hyperplasia of Eyelid

Sebaceous Glands of Eyelid, Tumors Arising in

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Synonyms

Chalazion; Sebaceous carcinoma; Sebaceous gland adenoma; Sebaceous gland hyperplasia

Definition

Sebaceous glands are holocrine glands that produce sebum, responsible for the outer portion of the tear film that prevents evaporation. Sebaceous glands in the periocular region include the meibomian glands of the tarsus, zeis glands of cilia, and the sebaceous glands of the caruncle. These glands can give rise to neoplastic transformation and infiltration. Specific lesions include sebaceous adenoma, sebaceous hyperplasia, chalazion, and sebaceous carcinoma (Shields and Shields 1999; Albert and Jakobiec 2008).

Characteristics

Rare outside the periocular region.

Sebaceous adenoma is a benign lesion with a yellow-fatty papillomatous appearance. Sebaceous gland lobules demonstrate incomplete differentiation on histopathology. Sebaceous adenoma has an association with Muir-Torre syndrome, an autosomal dominant condition associated with sebaceous tumors of the skin and visceral malignancies, often colon cancer.

Sebaceous gland hyperplasia is the enlargement of preexisting sebaceous lobules while maintaining the normal glandular architecture. There is no association with visceral tumors in sebaceous hyperplasia.

Sebaceous carcinoma is an aggressive tumor of the eyelid that causes loss of the normal eyelid architecture. Findings include madarosis, scarring or notching at the lid margin, and mass formation. It may mimic more benign conditions, such as blepharoconjunctivitis, cellulitis, and recurrent chalazions. It is has a tendency for recurrence and metastasis. Mortality has been reported around 30% over 5 years (Shields and Shields 1999; Albert and Jakobiec 2008).

Differential Diagnosis

Sebaceous gland adenoma
Sebaceous gland hyperplasia
Sebaceous carcinoma
Chalazion

Management

See individual entities for further information. Genetic testing may be indicated if Muir-Torre syndrome is suspected.

Cross-References

- ▶ Chalazion
- ▶ Sebaceous Carcinoma
- ▶ Sebaceous Gland Adenoma
- ▶ Sebaceous Gland Hyperplasia

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Sebaceous Glands of the Eyelid

▶ Glands of Krause, Glands of Moll, Glands of Wolfring, Glands of Zeis

Sebaceous Hyperplasia

▶ Sebaceous Hyperplasia of Eyelid

Sebaceous Hyperplasia of Eyelid

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Synonyms

Pseudoadenomatous hyperplasia; Sebaceous gland hyperplasia; Sebaceous hyperplasia

Definition

A benign growth of sebaceous gland lobules.

Etiology

Hyperplasia of holocrine glands of the eyelid that include meibomian glands, Zeis glands, and sebaceous glands of the caruncle. Sebaceous glands are androgen sensitive and as levels of androgens decrease with age, a hamartomatous enlargement of the sebaceous gland and sebaceous hyperplasia occurs. The lesions tend to maintain normal appearing sebaceous gland architecture (Shields and Shields 1999; Deplewski and Rosenfield 2000; American Academy of Ophthalmology 2006–2007; Albert and Jakobiec 2008).

Clinical Presentation

As multiple, small, white-yellow papules that may have central umbilication and telangiectasia. Lesions may be very similar to basal cell carcinoma in appearance; however, they tend to have a more yellowish color and be softer on palpation. It tends to present on the forehead and cheeks in middle age. Examples of sebaceous hyperplasia include rhinophyma of acne rosacea and the yellowish lobular masses sometimes seen on the caruncle (Shields and Shields 1999; American Academy of Ophthalmology 2006–2007; Albert and Jakobiec 2008).

Diagnostics

Excisional biopsy is not necessary; however, suspicious lesions should be excised to distinguish it from other lesions.

Differential Diagnosis

Acrochordon
Basal cell carcinoma
Milia
Molluscum contagiosum
Muir-Torre syndrome
Sebaceous adenoma
Sebaceous carcinoma
Syringoma
Trichoepithelioma
Trichofolliculoma

Prophylaxis

May recur if not completely excised.

Therapy

Benign therefore treatment is not mandatory. Suspicious lesions should be biopsied to distinguish it from other lesions. Options for excision include traditional excision, cryotherapy, photodynamic therapy, and laser and chemical treatments (Shields and Shields 1999; American Academy of Ophthalmology 2006–2007; Albert and Jakobiec 2008).

Prognosis

Excellent.

Epidemiology

Common finding, especially in adults, reported in approximately 1% of the population.

Cross-References

▶ Basal Cell Carcinoma of Eyelid
▶ Sebaceous Adenoma

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Seborrheic Blepharitis

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Synonyms

Blepharitis; Posterior blepharitis

Definition

Inflammation of the anterior portion of the eyelid, centered around the eyelashes and follicles.

Etiology

Abnormal oily secretions causing irritation to the eyelids.

Clinical Presentation

Seborrheic blepharitis is a type of inflammation of the anterior portion of the eyelid, centered around the eyelashes and follicles. The disease is the result of chronic abnormal oily secretions that cause irritation to the eyelids (Asbell and Lemp 2011). The eyelids are characterized by oily or greasy residue without any ulceration or loss of the eyelashes. Seborrheic blepharitis is associated with rosacea up to 33% of the time (External Disease and Cornea 2011).

Differential Diagnosis

Rosacea, staphylococcal blepharitis, and sebaceous carcinoma.

Prophylaxis

Warm compresses and lid hygiene.

Therapy

Lid hygiene, antibiotics, steroid eye drops or ointments, and artificial tears treat the underlying condition.

References

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Seborrheic Keratosis

► Papillomas, Eyelid

Secondary Angle Closure Glaucoma and Uveal Effusion

► Angle Closure Secondary to Uveal Effusion

Secondary Angle-Closure Glaucoma

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Definition

Secondary angle-closure disorders are all forms of angle-closure glaucoma that occur in the presence of a second ocular disease such as with iris

neovascularization, uveitis, trauma, or lens disease-related conditions (Allingham et al. 2005).

Etiology

The angle-closure mechanisms include situations in which the peripheral iris is in apposition to the trabecular meshwork or peripheral cornea (Rauscher and Parrish 2008). The peripheral iris may either be "pulled" (anterior mechanism) or "pushed" (posterior mechanism) into this position. In the anterior mechanism of angle-closure glaucoma, an abnormal tissue bridges the anterior chamber angle and subsequently undergoes contraction, pulling the peripheral iris into the iridocorneal angle. Examples of the contracting tissue include a fibrovascular membrane, an endothelial layer with a Descemet-like membrane, and inflammatory precipitates. In the posterior mechanisms, pressure behind the iris, lens, or vitreous causes the iris to be pushed into the anterior chamber angle. This may occur with or without pupillary block. In primary pupillary block glaucoma, functional apposition between the peripupillary iris and the lens increases resistance of aqueous humor flow into the anterior chamber, resulting in a relative increase in posterior chamber pressure and forward bowing of the peripheral iris. The functional apposition in these patients is due to a genetically determined configuration of the anterior ocular segment. In other (secondary) conditions, the same functional apposition between the lens and iris results from a forward shift of the lens (e.g., intumescent cataract or subluxated lens). In still other cases, a pupillary block may be due to posterior synechia associated with inflammation of the anterior ocular segment. In each of these conditions, apposition between the iris and the lens, intraocular lens, and vitreous obstructs the flow of aqueous humor into the anterior chamber, resulting in increased pressure in the posterior chamber and forward bowing of the peripheral iris into the anterior chamber angle. In the posterior mechanism of angle closure without pupillary block, increased pressure in the posterior portion of the eye pushes the lens-iris or vitreous-iris diaphragm forward. Examples include malignant (ciliary block) glaucoma, plateau iris syndrome, intraocular tumors, cysts of the iris and ciliary body, and contracture of retrolenticular tissue.

Clinical Presentation

The anterior mechanisms of secondary angle closure are seen in the angle-closure stage of neovascular glaucoma, in the group of iridocorneal endothelial (ICE) syndromes, in posterior polymorphous corneal dystrophy, in penetrating or nonpenetrating ocular trauma, and in cases where inflammatory precipitates in the chamber angle contract. In addition, it may play a significant role in patients with congenital aniridia (which usually is not total) and in patients with secondary glaucoma due to surgery of congenital cataracts.

Posterior mechanisms with pupillary block are seen in secondary angle closure due to lens-induced mechanism (intumescent, subluxated, or mobile lens) and in eyes with posterior synechia formation, in patients with iris-intraocular lens block in pseudophakia, uveitis with posterior synechia, and iris-vitreous block in aphakia (Tarongoy et al. 2009).

Posterior mechanisms without pupillary block are seen as secondary angle-closure glaucoma in malignant glaucoma, in lens-induced mechanism (intumescent,subluxated, or mobile), following lens extraction (forward vitreous shift), following scleral buckling surgery for retinal detachment, following panretinal photocoagulation, and following central retinal vein occlusion, in the presence of intraocular tumors such as malignant melanoma or retinoblastoma, in patients with cysts of the iris or ciliary body, and in cases where retrolenticular tissue is contracting (i.e., retinopathy of prematurity (retrolental fibroplasia) or persistent hyperplastic primary vitreous).

Diagnostics

To differentiate between these forms, a careful clinical investigation including slit-lamp

biomicroscopy, indirect binocular funduscopy, and careful gonioscopy is mandatory. Together with the history (especially previous intraocular surgeries), diagnosis may be obvious. Additional investigations include standard A- and B-mode ultrasound echography (to exclude tumors and the measure axial length and lens thickness) and high-resolution ultrasound biomicroscopy (UBM) to determine the anatomical relationship between the structures of the anterior segment (the chamber angle, iris, ciliary body, and lens). Ultrasound biomicroscopy is extremely helpful to differentiate between primary iris en plateau syndrome and secondary angle closure due to iris or ciliary body cysts. Additional tests should be used according to the diagnosis (i.e., specular microscopy in patients with presumed ICE syndrome)

Differential Diagnosis

There is a wide variety of differential diagnosis according to the various forms. In the anterior mechanism, ICE syndromes may be difficult to differentiate from posterior polymorphous corneal dystrophy. In these cases, specular microscopy has been shown to be especially helpful. The Axenfeld-Rieger syndrome has striking clinical and histopathologic similarities to the ICE syndrome, but the congenital nature and bilaterality help to separate these conditions. Some advanced cases of progressive iris atrophy might resemble aniridia, but the bilaterality of the latter disorder is a helpful differential feature.

In the posterior mechanisms, diagnosis of pupillary block is important. This may either be done by clinical investigations including UBM or *ex juvantibus* by performing a laser iridotomy and observing the changes in iris configuration and in the chamber angle thereafter. Laser iridotomy in cases with extensive posterior synechia formation may close soon due to extensive inflammatory response, and a surgical iridectomy with or without synechiolysis is indicated.

An important differential diagnosis is nanophthalmos. This is a rare, bilateral, sporadic, or familial condition characterized by small eyes, with adult axial lengths of less than 20 mm, shallow anterior chambers with narrow angles and convex irides, small corneal diameters, high hyperopia, thick sclera and choroid, high lens/eye volume ratio, high corneal refractive power, absence of other congenital malformations, and the frequent occurrence of angle closure.

Another important differential diagnosis is capsular bag distension syndrome, which occurs when a liquified substance (retained hyaluronic acid) accumulates within a closed lenticular bag, which usually forms when the IOL occludes or adheres to the anterior capsulorrhexis. Clinical features, evident 1–14 days postoperatively, include anterior IOL and iris displacement, causing myopia and anterior chamber shallowing. A narrow slit-lamp beam will identify a thin strip of posterior capsule, confirming the diagnosis.

If none of the abovementioned causes are found, a careful medical history may reveal the use of drugs that induce angle-closure glaucoma (Razeghinejad et al. 2011). Usually this is the case in patients with preexisting occludable angles, but especially sulfa drugs (topiramate, hydrochlorothiazide, acetazolamide), quinine, and tetracycline may cause a secondary angle closure without pupillary block. The mechanism is a swelling of the choroid and the ciliary body.

Prophylaxis

Laser peripheral iridotomy eliminates the pressure differential between anterior and posterior chambers and is the current standard treatment to correct pupillary block in the initial approach to angle closure. It is also a safe and effective prophylaxis in suspect eyes with occludable angles secondary to pupillary block. It is also regarded as prophylaxis in young patients with lens subluxation and will prevent the occurrence of acute angle closure. As the lens plays a significant role in the development of angle closure in secondary angle-closure glaucoma, lensectomy may be a logical step in prophylaxis. Cataract surgery in eyes with angle closure, however, carries a significantly increased risk of complications. Using modern cataract surgical techniques, the potential risk is minimized, and when the surgery is performed by an experienced

cataract surgeon, the benefits outweigh the risks in a majority of cases. A protective effect of lensectomy is obvious in patients with phacomorphic angle closure but may also be successful in patients with nanophthalmos and patients with angle closure due to retinopathy of prematurity.

Therapy

The therapy of secondary angle closure should be primarily focused on the mechanism of the angle closure but should also take the underlying disease into account. In those cases with anterior mechanisms, the causing disease should be treated. In a case with neovascular glaucoma, the stimulus for neovascularization should be minimized, and in patients with inflammatory disease, the uveitis should be aggressively treated. In addition to IOP-lowering medications, topical steroids and cycloplegic agents may improve the situation. In the posterior mechanisms with pupillary block, a laser or surgical iridectomy is mandatory. If extensive posterior synechia is present, synechiolysis either medically or surgically will improve the situation. If the anterior hyaloid face is blocking the pupil, an anterior vitrectomy together with a surgical iridectomy will probably be required as a laser iridotomy may be blocked too easily. In posterior mechanism without pupillary block, maximal cycloplegia and hyperosmotic agents may be able to reverse the vicious circle. Using argon laser peripheral iridoplasty may be favorable in some of the above situations but may not be curative. Before any form of filtering glaucoma surgery is necessary, lensectomy should be performed, or a combined procedure may be preferred.

Prognosis

Prognosis is much dependent on the underlying disease, but as some of these secondary angle-closure glaucomas are rare, exact diagnosis may be missed and adequate treatment delayed. Early diagnosis and appropriate treatment may cure the majority of cases.

Epidemiology

Because there is such a variety in diagnoses and underlying diseases, no epidemiologic data are available.

Cross-References

- ▶ Aniridia, Traumatic
- ▶ Aphakic Spectacles
- ▶ Axenfeld-Rieger Syndrome; Mesodermal Dysgenesis; Leukomas
- ▶ Capsular Bag Distension Syndrome
- ▶ Central Retinal Vein, Occlusion of
- ▶ Ciliary Body
- ▶ Conjunctival Tumors
- ▶ ICE Syndrome
- ▶ Lens-Induced Angle-Closure Glaucoma
- ▶ Malignant Glaucoma
- ▶ Malignant Melanoma (MM)
- ▶ Nanophthalmos
- ▶ Neovascular Glaucoma in VOR
- ▶ Persistent Hyperplastic Primary Vitreous
- ▶ Photocoagulation
- ▶ Posterior Polymorphous Corneal Dystrophy
- ▶ Retinoblastoma
- ▶ Retinopathy of Prematurity
- ▶ Scleral Buckle
- ▶ Secondary Glaucoma in Uveitis
- ▶ Sulfur Hexafluoride (SF6)
- ▶ Uveitic Glaucoma

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Secondary Anterior Crocodile Shagreen of Vogt

▶ Mosaic Degeneration (Anterior Crocodile Shagreen)

Secondary Blepharospasm

▶ Reflex Blepharospasm

Secondary Cataract

▶ Capsular Bag Opacification

Secondary Glaucoma in Uveitis

▶ Other Uveitic Etiologies

Secondary Glaucoma in Uveitis/ Inflammatory Eye Disease

▶ Uveitic Glaucoma

Secondary Open-Angle Glaucoma

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Definition

A secondary open-angle glaucoma is a glaucoma caused by a separate ophthalmic or systemic disease and showing an open anterior chamber angle.

Etiology

Etiology depends on the subtype of secondary open-angle glaucoma.

Diagnosis

Diagnosis of a secondary open angle glaucoma should be based on slit-lamp biomicroscopy, ophthalmoscopy, gonioscopy, and perimetry.

Differential Diagnosis

Differential diagnosis includes primary open-angle glaucoma, secondary angle closure glaucoma, and congenital glaucoma.

Prophylaxis

Treatment of the underlying disease before glaucoma occurs.

Therapy

Whenever possible therapy should start with treatment of the underlying disease, followed by medical or surgical intraocular pressure reduction.

Prognosis

Prognosis strongly depends on successful intraocular pressure reduction.

Epidemiology

About 10% of all glaucomas are secondary open-angle glaucomas.

Cross-References

▶ Aphakic Spectacles
▶ Axenfeld-Rieger Syndrome; Mesodermal Dysgenesis; Leukomas

- ▶ Corticosteroids
- ▶ Pigmentary Glaucoma
- ▶ Pseudoexfoliative Glaucoma
- ▶ Traumatic Glaucoma
- ▶ Uveitic Glaucoma

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Sed Rate

- ▶ Erythrocyte Sedimentation Rate in Giant Cell Arteritis

Semicircular Advancement Flap

- ▶ Semicircular Flap for Eyelid Repair
- ▶ Tenzel Flaps

Semicircular Flap

- ▶ Semicircular Flap for Eyelid Repair
- ▶ Tenzel Flaps

Semicircular Flap for Eyelid Repair

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Synonyms

Local advancement flap; Semicircular advancement flap; Semicircular flap; Semicircular temporal advancement flap; Tenzel advancement flap

Definition

A semicircular local advancement flap is often utilized in the reconstruction of full thickness eyelid defects. It allows recruitment of tissues lateral to the lateral canthus and medial mobilization of the eyelid to allow direct wound closure.

Indication

Semicircular advancement flap is indicated in the reconstruction of upper or lower full thickness eyelid defects involving approximately 1/3 to 1/2 of the eyelid. The Tenzel advancement flap is most commonly employed in reconstruction following resection of a neoplasm at the eyelid margin, or in cases of trauma with full thickness tissue loss.

Contraindications

The defect size and laxity of the individual patient's tissues dictate which reconstructive options are available to the surgeon. Large defects, usually greater than 50% of full thickness eyelid, require reconstructive techniques other than a semicircular advancement flap to allow recruitment of adequate tissue for reconstruction.

Techniques and Principles

The eyelid defect is assessed and the appropriate reconstructive technique determined. Full thickness eyelid defects encompassing approximately 1/3 to 1/2 of the eyelid, and having intact eyelid structures at the lateral canthus which can be advanced medially, are generally good candidates for reconstruction with a Tenzel flap. A semicircular flap of appropriate size is marked beginning at the lateral canthus. The flap typically extends approximately 1/2 to 2/3 of the distance from the lateral canthus to the hairline depending on the extent of advancement required. The flap is created with a superior semicircular incision and rotated inferiorly or conversely and created with an inferior semicircular incision and rotated superiorly for lower and upper eyelid defects, respectively.

Lateral canthotomy in combination with cantholysis are performed to free the lateral eyelid and allow mobilization nasally. The wound margins are apposed by direct closure in a standard fashion for full thickness eyelid repair ensuring that excess tension on the wound has been relieved via mobilization of the lateral eyelid segment. Suturing the flap to the orbital rim periosteum forms the lateral lid contour. The lateral canthus is fixated and the conjunctiva is undermined and advanced to the flap edge if necessary.

Outcome

A semicircular incision extending temporally from the lateral canthus with reconstruction of the full thickness eyelid defect is the final result. The lateral most aspect of the reconstructed eyelid will be devoid of eyelashes secondary to the medial advancement of the eyelid tissues formerly residing at the lateral canthal region.

Complications

Excess tension on the newly reconstructed full thickness eyelid defect can result in wound dehiscence. Phimosis and rounding of the lateral canthus can occur with healing particularly if excess wound tension is present. Damage to the zygomatic branch of the facial nerve with resultant orbicularis occuli weakness secondary to deep dissection in the lateral canthal region.

Cross-References

- ▶ Cantholysis
- ▶ Canthotomy
- ▶ Eyelid Reconstruction
- ▶ Lateral Canthal Reconstruction

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Semicircular Temporal Advancement Flap

- ▶ Semicircular Flap for Eyelid Repair
- ▶ Tenzel Flaps

Semilunar Ganglion

- ▶ Gasserian Ganglion (Semilunar/Trigeminal Ganglion)
- ▶ Trigeminal Ganglion (Gasserian/Semilunar Ganglion)

Senile Furrow

- ▶ Furrow Degeneration, Senile

Senile Hyperkeratosis

- ▶ Actinic Keratosis

Senile Keratosis

- ▶ Actinic Keratosis
- ▶ Actinic (Solar) Keratosis

Senile Marginal Atrophy

- ▶ Furrow Degeneration, Senile

Senile Marginal Degeneration

- ▶ Furrow Degeneration, Senile

Septal Fat Pannus

► Sub-brow Fat Pads

Septic Thrombosis of Orbital Veins

► Thrombophlebitis, of Orbital Vein

Serous Detachment of the Sensory Retina

► Subretinal Fluid

Setting Sun Sign

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Synonyms

Downward Ocular Deviation; Sunset Eye Sign

Definition

The "setting sun" sign is an ophthalmologic phenomenon where the eyes appear driven downward bilaterally. The inferior border of the pupil is often covered by the lower eyelid, creating the "sunset" appearance. This finding is classically associated with hydrocephalus in infants and children.

Etiology

The pathogenesis of the setting sun sign is believed to be related to aqueductal distention in the dorsal midbrain on the vertical gaze innervation bilaterally. In children with hydrocephalus, up to 40% of cases will present with this sign. Of these patients, 13% harbor ventriculoperitoneal shunts that have failed. The sign is also associated with kernicterus and other features of the full Parinaud syndrome (i.e., dorsal midbrain syndrome). Interestingly, the setting sun sign may also transiently appear in healthy infants up to 7 months of age. This benign phenomenon is believed to be caused by immaturity of reflexes controlling eye movements.

Clinical Presentation

Patients with setting sun sign present with bilateral up-gaze paresis, with the eyes appearing to be driven downward. The superior sclera is largely exposed between the upper eyelid and the iris. The inferior iris and pupil may be partially covered by the inferior eyelid. This condition may be persistent or transient.

Diagnostics

The setting sun sign is often a marker of hydrocephalus. Thus, whether the condition is persistent or transient, patients must be assessed for ventricular obstruction, failed ventriculoperitoneal shunts, lesions and/or tumors of the midbrain and periaqueductal structures, or other causes of increased intracranial pressure via

ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), or intracranial pressure-monitoring techniques. Bilirubin levels could be performed in cases of suspected kernicterus.

Differential Diagnosis

Kernicterus
Hydrocephalus
Shunt failure
Transient benign finding in infants

Therapy

Treatment should be directed at the underlying etiology.

Prognosis

The prognosis of the setting sun sign in patients is dependent on the etiology. The most common cause, hydrocephalus, is a potentially life-threatening condition and even if successfully treated can result in permanent brain injury. However, the setting sun sign is often the earliest marker of elevated intracranial pressure in children, and with quick diagnosis and treatment, permanent neurological damage can be minimized.

Epidemiology

The sign is often seen in children especially those with shunted hydrocephalus.

Cross-References

- ▶ Dorsal Midbrain (Parinaud) Syndrome, Convergence-Retraction Nystagmus, Eyelid Retraction
- ▶ Parinaud's Syndrome
- ▶ Vertical gaze palsy

Further Reading

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Seventh Nerve Palsy

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Synonyms

Bell palsy; Facial nerve palsy

Definition

Seventh nerve palsy is classified into two distinct categories, central lesions and peripheral lesions. Central lesions involve upper motor neurons, while peripheral lesions involve lower motor neurons and will present with slightly different symptoms and signs. Upper motor neurons extend from

the precentral gyrus of the cerebral cortex and descend through the brainstem via corticobulbar tracts to synapse at lower motor neuron cranial nerve seven (VII) nuclei in the pons. The musculature of facial expression above the eyebrow is innervated bilaterally, while the musculature of facial expression below the eyebrow is innervated contralaterally. Depending on the level of the lesion, symptoms can include weakness or paralysis of musculature of facial expression, loss of lacrimation and salivation, hyperacusis, and loss of taste from the anterior two-thirds of the tongue.

Clinical Features

Central lesions manifest as weakness or paralysis in the lower facial musculature below the eyebrow with the ability to close the upper eyelid and wrinkle the forehead intact. Peripheral lesions manifest as weakness or paralysis in the facial musculature above and below the eyebrow. In both categories, patients can present with flattened nasolabial folds, drooping of the corner of the mouth, paralytic ectropion, or lagophthalmos. Patients may also display decreased lacrimation and salivation, hyperacusis, and loss of taste from the anterior two-thirds of the tongue. Later in the course, patients may display cranial nerve VII aberrant regeneration and synkinesis.

Tests

After a complete history is taken, a thorough neurological exam to determine if the condition is a central or peripheral palsy and if it is complete or incomplete is necessary. Test for taste sensation to the anterior two-thirds of the tongue and assess functioning of other cranial nerves. A complete ocular exam is required for ocular motility and nystagmus. Otolaryngologic examination is required to assess the ear and oropharynx for lesions, to assess the parotid gland for possible lymphadenopathy, and to assess hearing. Computed tomography (CT) scans are required if there is a history of trauma, and CT and magnetic resonance imaging (MRI) scans may be required if there are any other localizing signs or a history of cancer. If sarcoidosis is suspected, a chest radiograph and angiotensin-converting enzyme levels could be performed. If collagen vascular disease is suspected, rheumatoid factor, erythrocyte sedimentation rate, antinuclear antibody, and antineutrophil cytoplasmic antibody tests could be performed. Depending on the clinical presentation, Lyme titer, Epstein-Barr virus titer, RPR, HIV test, and CBC with differential may be performed.

Differential Diagnosis

- Myasthenia gravis
- Lyme disease
- Sarcoid

Etiology

Central lesions can be cortical, extrapyramidal, and in the brainstem. Cortical lesions often occur because of stroke or tumor. Extrapyramidal lesions of the basal ganglia often occur from parkinsonism, a vascular lesion, or tumor. Brainstem lesions can occur from multiple sclerosis, stroke, or tumor. Peripheral lesions involving lower motor neurons can be found in the cerebellopontine angle from masses such as acoustic neuromas, facial neuromas, meningiomas, cholesteatomas, and metastasis. Trauma and otitis can also be causes for peripheral seventh nerve palsy. Other conditions that may cause symptoms of peripheral seventh nerve palsy include Ramsay Hunt syndrome, Guillain-Barre syndrome, Lyme disease, sarcoidosis, parotid neoplasm, metastasis, diabetes mellitus, botulism, human immunodeficiency virus, syphilis, Epstein-Barr virus, acute porphyrias, nasopharyngeal carcinoma, and collagen-vascular disease.

Treatment

Treatment should be directed at the underlying etiology. Exposure keratopathy management might include artificial tears and lubricating ointment and, in extreme cases, eyelid gold weight or spring implants to aid in eyelid closure.

Cross-References

- ▶ Bell's Palsy
- ▶ Facial Nerve Palsy

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Severe Anterior Segment Dysgenesis

- ▶ Sclerocornea

Sexually Transmitted Disease

- ▶ Syphilis: Overview

Shack-Hartmann Aberrometry

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Synonyms

Hartmann-Shack wave front sensing

Definition

Non-interferometric wave front aberrometer.

Purpose

Measuring the optical path of light rays through the eye to detect all aberrations at all points in the optical system of the human eye.

Principle

The Hartmann-Shack wave front sensor is used to measure the wave aberrations of the human eye by sensing the wave front emerging from the eye produced by the retinal reflection of a focused light spot on the fovea. It comprises a microlenslet array subdividing the reflected wave of light into multiple focused beams. The incident plane wave results in a square grid of spots captured by an image detector in the focal plane of the lenslet array. The distorted wave front causes lateral displacements of the spots on the CCD array. Thus, from the spot pattern, the shape of the incident wave front can be reconstructed (Bille 2000; Bille et al. 2004).

Indication

Measurement of the aberrations of the eye, correlation with visual symptoms, wave front sensing for preoperative evaluation of refractive surgical procedures.

Contraindication

None.

Advantage/Disadvantage

Shack-Hartmann aberrometry employs the fastest technique compared to other wave front sensing devices. Yet, if the grid of image spots is too distorted, indexing problems may be experienced (i.e., the boundary between adjacent spots is not clear). The use of a laser light source can produce an undesirable speckle effect in a Shack-Hartmann sensor. This speckle noise can affect the precision and accuracy of the wave front sensor measurement and limited number of pixels.

As a fixed monolithic microlenslet array is used, the sampling configuration cannot be modified unless different microlens arrays are used. Shack-Hartmann aberrometers rely on a good retinal reflection, which can be a problem in retinal pathologies (Moreno-Barriuso et al. 2001; Wang et al. 2003).

Cross-References

- ▶ Aberrometry
- ▶ Higher-Order Aberrations, Refractive Surgery
- ▶ Ray Tracing
- ▶ Wave Front Analysis

References

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Shadow Image

- ▶ Monocular Diplopia

Shagreen, Crocodile

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Synonyms

Valerio's mosaic degeneration; Vogt's crocodile shagreen dystrophy

Definition

Initially described in 1927 by Weizenblatt and named by Vogt in 1930, crocodile shagreen is an opacification of the cornea characterized by a mosaic-like arrangement of polygonal, gray opacities separated by clear zones, resembling cobblestone or crocodile skin. There are anterior and posterior forms of the degeneration, which will be discussed in greater detail below.

Etiology

The anterior form of crocodile shagreen is most often due to senile change, but has also been associated with hypotony, trauma, band keratopathy, pseudoxanthoma elasticum, glaucoma, polymorphic amyloid degeneration, and juvenile X-linked megalocornea. Similar changes have also been described in patients with keratoconus who wear hard contact lenses, as well as with fluorescein staining of the cornea after pressure is patched. The posterior form, however, has been described solely as an age-related degeneration.

Occurrence

The anterior form of the degeneration usually occurs bilaterally and centrally, whereas the posterior form may occur peripherally, occasionally resembling corneal arcus. The opacities are usually visually insignificant and require no treatment.

Classification

As stated above, both anterior and posterior forms of crocodile shagreen exist. Anterior crocodile shagreen is generally a central corneal opacity at the level of Bowman layer. Histologically, the Bowman layer is thrown into ridges, and calcium may be deposited at the peaks of the folds. Posterior crocodile shagreen shows similar sawtooth folds in the deep stroma near Descemet's

membrane. The posterior variety of crocodile shagreen is clinically identical to central cloudy dystrophy of François, though the latter occurs in an autosomal dominant pattern and does not typically extend to the periphery.

Cross-References

► Central Cloudy Dystrophy of François

Further Reading

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Shave Biopsy

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Definition

Shave biopsy is the removal of a superficial skin lesion for diagnostic or therapeutic reasons.

Purpose

A shave biopsy serves to diagnose and at times provide definitive treatment for superficial skin conditions.

Principle

Choosing the appropriate site for biopsy is key in yielding diagnostic potential (Alguire and Mathes 1998). For inflammatory lesions, it is generally recommended to biopsy lesions in the advanced stages of inflammation. On the other hand, for blistering lesions, the earlier the lesion, the better for biopsy. For lesions 1–4 mm in diameter, biopsy the middle or excise the whole lesion. For larger lesions, biopsy the thickest part, the edge, or the area with most abnormal color. Vesicles and bullae should be biopsied with the lesion edge intact.

To perform the procedure, first obtain informed consent from the patient (Pickett and O'Callaghan 2011). Next clean the area using povidone-iodine or chlorhexidine. Next anesthetize the skin using lidocaine. For macular or raised non-suspicious lesions, carefully remove a shallow, thin disk of lesion or the entire lesion itself by meticulously holding the blade parallel to the skin. For suspicious, pigmented, raised lesions, saucerization may be performed. This entails anesthetizing the lesion to create a wheal and pinching the area to facilitate the biopsy. Rather than holding the blade parallel like in a classic shave biopsy, in saucerization, the blade is held at a 45° angle to the skin; the blade is bent or bowed depending on the lesion size, and a disk of tissue is removed. If pigment still remains after saucerization, a punch biopsy may be performed to remove and examine the remaining pigment.

Indication

Cutaneous lymphoma, deep tissue infection, dysplastic nevi, erythema multiforme, erythema nodosum, Kaposi sarcoma, lupus erythematosus, malignant melanoma, panniculitis, pemphigoid, pemphigus, and vasculitis.

Contraindication

If the lesion is located on challenging areas, e.g., the eyelids and nose, the patient should be referred

to an oculoplastic surgeon or dermatologist to prevent an aesthetically undesired scar. Usually biopsies should not be done at an infection site, unless the infection of the lesion is the indication for the procedure. Since the shave biopsy procedure involves the use of topical anesthetics, any adverse medical reactions to the topical agents used may be a contraindication. Lastly, if a patient has a bleeding disorder or is taking warfarin or another anticoagulant, the patient should be referred to an oculoplastic surgeon or dermatologist for the procedure.

Advantages/Disadvantages

Shave biopsies can be performed in the urgent care or clinic setting with appropriate equipment. When performed properly, shave biopsies can yield clinically useful information and provide definitive therapy for superficial, small lesions.

Shave biopsies are ideally not performed in areas with poor healing. These include cosmetic areas, e.g., eyelids and the nose, or deltoid and chest area, where hypertrophic scarring occurs. Biopsies over the tibia can be an issue for patients with poor wound healing, e.g., diabetics and patients with arterial or venous insufficiency. Lastly, biopsies in the groin or axilla are prone to secondary infections.

Cross-References

▶ Biopsy

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Shingles

▶ Herpes Zoster
▶ Postherpetic Neuralgia

SIA

▶ Surgically Induced Astigmatism

Sicca Syndrome

▶ Keratoconjunctivitis: Overview

Sickle Cell Anemia

▶ Comma Sign, in Sickle Cell Hemoglobinopathies

Sickle Cell Disease

▶ Comma Sign, in Sickle Cell Hemoglobinopathies

Sickle Cell Retinopathy

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Definition

Sickle cell retinopathy describes the progressive retinal changes of both a nonproliferative and proliferative nature, which occur secondary to sickle cell disease.

Etiology

Sickle cell anemia is a hemoglobinopathy characterized by the production of abnormal erythrocytes, which become rigid and take up a sickle shape exacerbated by hypoxia or acidosis. This leads to red cell membrane damage and hemolysis. Normal hemoglobin comprises a central heme ring with tertiary conformation by two surrounding

pairs of globin polypeptides chains. Hemoglobinopathies and thalassemias occur as a consequence of alterations in the amino acid composition of globin chains or the rate of their production. The most prevalent sickle genotype is HbS and is caused by a single nonconservative missense mutation in the β -globin chain (glutamic acid > valine). Inheriting this mutation from both parents results in homozyosity for Hb S, designated as Hb SS. A number of hemoglobin variants exist, e.g., Hb C, E, D, O, and G. Inheriting different mutations from parents can result in a compound heterozygous state as seen in Hb SC, where the Hb S variant is inherited from one parent and Hb C from the other parent. The Hb SC genotype is the commonest compound heterozygous state. Carriers of Hb S with one normal allele are known as Hb AS (Tibbets and Ho 2013).

Sickle cell retinopathy results from repeated vaso-occlusion and adhesion of the sickled erythrocytes to the vascular endothelium, particularly in locations where both arterial PaO_2 and pH are lower, as in the small capillaries of the peripheral retina. Sickle cell carriers generally have limited systemic disease and minimal evidence of retinopathy unless they have co-morbidity such as diabetes. However, Hb SS or the compound heterozygous state, e.g., Hb SC, or Hb AS together with β thalassemia, or Hb SS with α thalassemia, will usually lead to ocular disease manifestations, and the compound heterozygotes state is associated with earlier onset of retinal neovascularization and visual complications, whereas patients with homozygous sickle cell disease, e.g., Hb SS, tend to have more severe systemic disease but milder retinal disease (Emerson et al. 2006).

Clinical Presentation

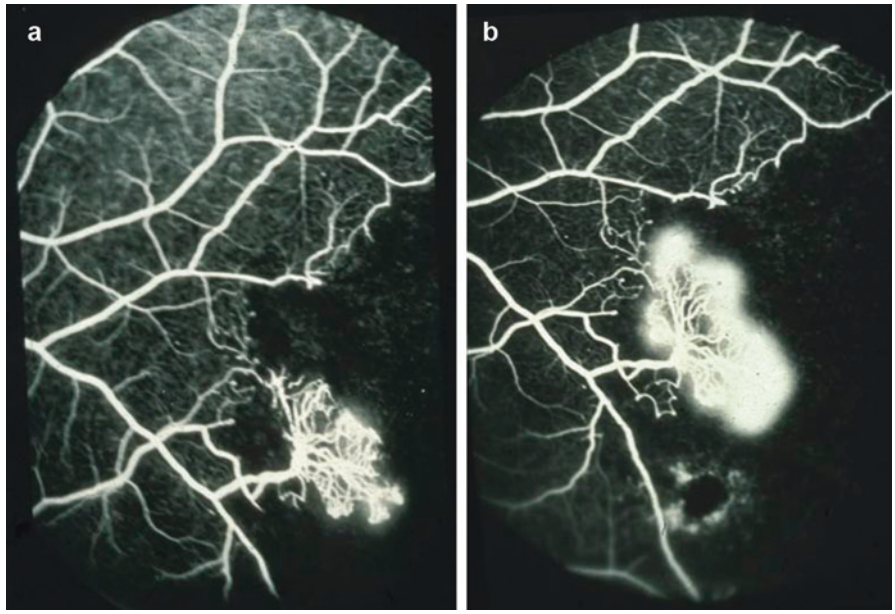
Most patients will be referred for ophthalmology screening after receiving a diagnosis of sickle cell disease. Due to the early changes occurring in the far periphery of the retina, patients will rarely notice any visual disturbance unless proliferative sickle retinopathy develops. Nonproliferative findings, which may be seen in the retina of a patient with sickle cell disease, can include:

1. Increased vessel tortuosity and vascular remodeling caused by peripheral vascular obstructions and reperfusions. Over the years, the centripetal band of ischemia progresses posteriorly, and "silver wiring" of vessels can be seen in areas of non perfusion.
2. Central retinal arterial obstruction.
3. Macular depression sign representing atrophy and thinning of the neural retina. Macular infarctions can occur.
4. Choroidal vascular occlusions, posterior ciliary arterial obstructions.
5. Epiretinal membranes and macular holes – more commonly in patients with previous or current neovascularization and/or laser treatment.
6. Salmon patches: retinal hemorrhages – traditionally called salmon patches due to their characteristic orange-red color after the acute phase, hemorrhages typically result from obstruction and subsequent rupture of intermediate-sized retinal arterioles.
7. Schitic cavities which occur after reabsorption of salmon patches.
8. Black sunbursts – these pigmented round lesions represent migration and hyperplasia of the underlying retinal pigment epithelium and may represent reactive proliferation after hemorrhage.
9. Iridescent spots – glistening copper-colored granules, which are the breakdown products of intraretinal blood.
10. Angioid streaks.

Goldberg classified sickle cell retinopathy in five stages:

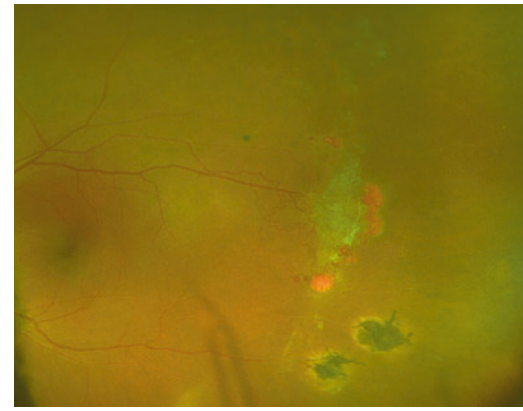
Stage I: Peripheral arteriolar obstructions
Stage II: Peripheral arteriolar-venular anastomoses
Stage III: Preretinal neovascularization – sea-fan neovascularization (Fig. 1)
Stage IV: Vitreous hemorrhage
Stage V: Retinal detachment (either rhegmatogenous, tractional, or combined) (van Meurs et al. 2007)

Signs of sickle cell retinopathy have been reported as early as 8 years of age, but the natural history of proliferative sickle retinopathy (PSR) is



Sickle Cell Retinopathy, Fig. 1 (**a**) and (**b**) Images of a sea fan developing over the interval of a year (Courtesy of Bird/Sarjent Sickle cell unit Jamaica)

that it peaks from 20s to early 40s then seems to plateau and is uncommon before teenage years. PSR is characterized by the growth of seafans, which develop in the ischemic peripheral retina in a circumferential distribution. A proportion of these will autoinfarct. This is a dynamic process and seafans may take years to close with new areas becoming active. A major cause of visual loss in PSR is vitreous hemorrhage, which may be recurrent and can spontaneously reabsorb, but in some cases, membranes may persist. Other than arterial obstructions and macular infarctions, the main cause of permanent visual loss is due to retinal detachments either untreated or with a poor outcome. Combined tractional and rhegmatogenous retinal detachments can occur in the thin non perfused retina adjacent to, or affected by, fibrosing seafans (Downes et al. 2005) (Figs. 2 and 3).



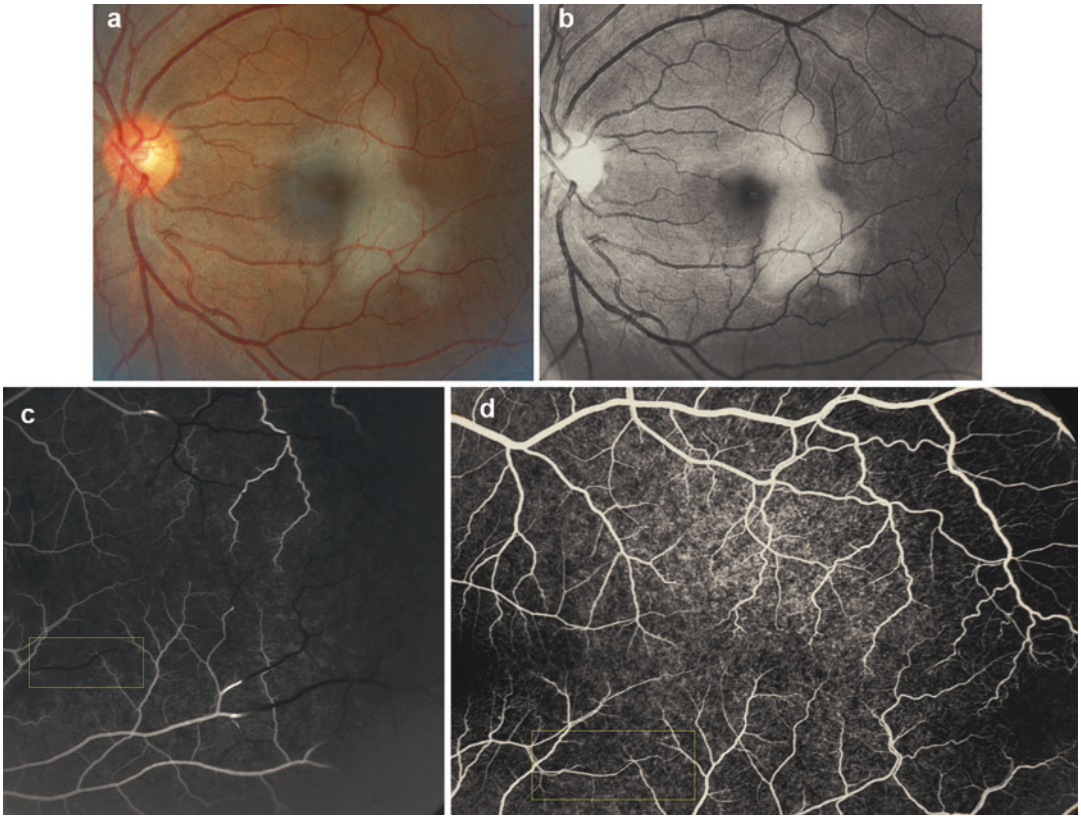
Sickle Cell Retinopathy, Fig. 2 Showing fibrosing seafan with active tips and bleeding and two *black* sunburst patches inferiorly with silver wiring of occluded vessels in the peripheral retina

Diagnosis

Sickled erythrocytes can be seen on blood smear microscopy and confirmed through hemoglobin electrophoresis. DNA analysis can identify the causative mutation. Diagnosis and assessment of proliferative sickle retinopathy is best visualized using fluorescein angiography.

Differential Diagnosis

Retinopathy of prematurity
Familial exudative vitreoretinopathy



Sickle Cell Retinopathy, Fig. 3 (**a**) Color image of macula showing ischemic macula due to obstruction of retinal arterioles, (**b**) *red* free image showing the extent of the ischemia with foveal sparing. (**c**) Areas of obstructed vessels. One vessel in *yellow* box is re-imaged 2 weeks later. (**d**) Showing reperfusion of same vessel seen in 2c, demonstrating the constant remodeling of the retinal vasculature in sickle retinopathy (Images courtesy of Alan Bird and Kingston Sickle Unit)

Retinal vasculitis
Branch retinal vein occlusion
Proliferative radiation retinopathy
Proliferative diabetic retinopathy
Eales' disease

Prophylaxis

Laser treatment has been used aiming at reducing the frequency of vitreous hemorrhages and inducing regression of PSR. As seafans can autoinfarct, and laser treatment is aimed at PSR closure, the evidence that laser prevents development of retinal detachments is not clear, but it can prevent vitreous hemorrhages. Targeted retinal photocoagulation can be used to treat retinal ischemia anterior to the seafans and has been shown to induce regression of PSR. Alternatively, a 360 laser to the anterior circumferential ischemic zone can be applied to prevent further neovascularization. Direct feeder vessel photocoagulation, where high-power laser is administered to the feeding arteriole, is not recommended and can be associated with significant complications including chorioretinal or choriovitreal anastamoses. Careful assessment of the peripheral retina on a regular basis, when PSR is present, is important for early detection and management of a retinal detachment. Patients should also be educated regarding retinal detachment symptoms, so that if they occur they need to be seen on an urgent basis (Elagouz et al. 2010).

Therapy

Surgery should generally be reserved for those with recurrent vitreous hemorrhage (>6 months), retinal detachment, and significant epiretinal membranes and macular holes. Modern vitrectomy techniques and even buckling procedures have been associated with positive visual outcomes. Good control of intraocular pressure, good hydration, oxygenation, and maintenance of body temperature during any procedure is imperative (Chen et al. 2014).

Prognosis

Visual prognosis is dependent on the variant of sickle cell disease. Compound heterozygous disease SC is associated with the most frequent and severe ocular manifestations, and severe visual loss is commoner in this group. Visual loss is most commonly due to recurrent vitreous hemorrhage and retinal detachment.

Epidemiology

Prevalence of sickle cell trait reaches approximately 20% in some regions of Africa and 8% in African-Americans. Men and women are equally affected. The development of PSR is dependent on genotype and age, with the highest risk period from 20 to 34 years in SC and the 40–50 years age group in SS.

Cross-References

- ▶ Angiography, Fluorescein
- ▶ Argon Laser Photocoagulation
- ▶ Laser Focal Treatment
- ▶ Neovascularization, Retinal

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Siderosis

- ▶ Iron, Corneal Intraocular Foreign Body of
- ▶ Siderosis: Signs and Symptoms

Siderosis Bulbi

- ▶ Siderosis: Signs and Symptoms

Siderosis: Signs and Symptoms

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Synonyms

Ocular siderosis; Siderosis; Siderosis bulbi

Definition

Siderosis is a degeneration of specific ocular tissues as a result of intraocular trivalent iron ion deposits (Davidson 1933). Signs of siderosis include dilated pupil (early), constricted visual field (late), cataract, glaucoma, iris heterochromia, and anisocoria due to a mydriatic and poorly reactive pupil in the affected eye (Yamaguchi and Tamai 1989). Symptoms may include decreased night vision, decreased color vision, and decreased visual acuity.

The classical clinical description of siderosis includes a rusty brown discoloration of the iris and a yellow-brown discoloration of the lens with deep brown opacities in the peripheral subcortical area (Spalton et al. 1994). Patients may recall a history of trauma to the eye or an occupation involving metal work (Ballantyne 1954).

Etiology

Siderosis is primarily caused by retained intraocular foreign bodies containing iron. Iron deposits in ocular tissues include the iris and its musculature, retina, anterior lens capsule, cornea, optic nerve, and trabecular meshwork (Ballantyne 1954). Electron microscopy of enucleated eyes with siderosis has shown ferritin particles deposited within the cytoplasm, in intracellular vacuoles (siderosomes) and within cell nuclei (Tawara 1986). There have been reports of retained iron-containing intraocular foreign bodies that did not cause siderosis (Lim et al. 2011). Characteristically, electroretinogram (ERG) shows an initial increase in the a-wave followed by flattening of the b-wave providing an objective way of following retina function over time (Mester and Kuhn 2002). Vitreous hemorrhage has also been known to cause changes consistent with siderosis (Ballantyne 1954). Additionally, a rare autosomal recessive disease called aceruloplasminemia results in iron overload in certain tissues including the retina leading to a clinical picture similar to siderosis (Dunaief et al. 2005).

Occurrence

Siderosis is rare. In a report of 40 patients with intraocular foreign bodies from two orbital surgery departments, only one had an iron-containing foreign body and follow-up indicated no signs of siderosis (Fulcher et al. 2002).

Classification

Siderosis, a type of metallosis, is a degenerative process secondary to iron exposure, most frequently traumatic in nature.

Cross-References

- ▶ Anisocoria
- ▶ Cataract, Causes and Treatment
- ▶ Nyctalopia: Night Blindness

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Silicone Intraocular Lens

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Synonyms

Silicone IOL

Definition

An intraocular lens that is made of silicone (polysiloxane).

Epidemiology

Of all implanted IOLs, silicone material accounts for about 5%.

History

After the first experimental studies by A. D. Ruedemann in the 1970s, silicone has been used as an IOL material since the early 1980s with Food and Drug Administration (FDA) approval obtained in 1990. The first silicone IOL had a refractive index of 1.41.

Clinical Features

Advantages of IOLs made of silicone are that they are heat resistant, autoclavable, moldable, compressible, highly transparent to visual light, and very flexible and provide good tensile and tear strength. Their disadvantages are that they are slippery, which makes them more difficult to manipulate, can be pitted, have a lower refractive index than acrylic lenses which refers to a higher thickness, and show high adherence to silicone oil after vitreoretinal surgery (Findl et al. 2010; Kohnen et al. 1995). Silicone's angle of water contact is 99°, which makes it more hydrophobic compared to hydrophobic acrylic IOLs that show an angle of water contact of 73°. Latest generations of silicone IOLs have a higher refractive index (1.41–1.46) and thus, thinner optics.

Tests

Good biocompatibility of silicone IOLs has been shown in numerous studies (Werner 2008).

Differential Diagnosis

Other IOL materials are polymethylmethacrylate (PMMA) or hydrophilic/hydrophobic acrylic.

Etiology

The term "silicone" refers to "silicon ketone" and was coined by F. S. Kipping to describe polydiphenylsiloxane by analogy of its formula Ph_2SiO.

Treatment

Silicone IOLs come as one-piece or three-piece IOLs and as monofocal, multifocal, and toric IOLs.

Cross-References

▶ Acrylic Intraocular Lens
▶ Foldable Intraocular Lens
▶ Intraocular Lens
▶ Polydimethylsiloxane
▶ Silicone Oil Tamponade

References

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Silicone Intubation

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Synonyms

Bicanalicular intubation; Lacrimal stents; Lacrimal tubes

Definition

Silicone intubation is performed by placing a tube through the lacrimal system. Placement of a silicone tube as part of various procedures of the tear drainage system is thought to increase success rate by maintaining patency of surgical created passages (Table 1).

Indications

The duration that the silicone tubes left in place varies based on surgeon preference and surgery type. Tubes are typically left in place for 3 months and then removed either in the office setting or under sedation.

Silicone Intubation, Table 1 Surgical indications for silicone stenting by anatomic location in the nasolacrimal system

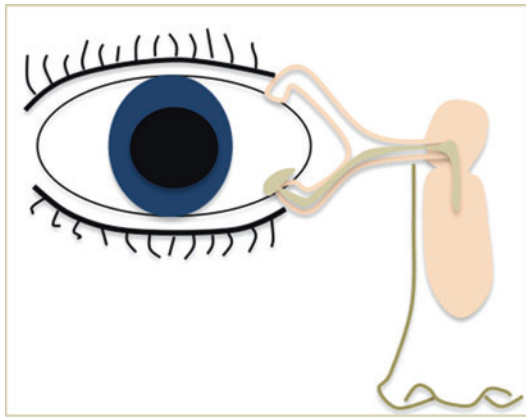
Punctum	Canaliculus	Nasolacrimal duct
Punctoplasty	Canalicular trauma repair	External dacryocystorhinostomy (DCR)
Punctal reconstruction	Canalicular recanalization	Endoscopic dacryocystorhinostomy (eDCR)
	Canaliculotomy	Balloon catheter dacryoplasty
		Nasolacrimal duct probing
		Turbinate infracture
		Silicone intubation (for functional NLDO)

Debate in the literate exists as to the benefit of using intubation devices for routine endoscopic and external DCR. Chong et al. conducted a randomized clinical study in patients undergoing endoscopic DCR and found no difference in success rates when silicone stent was utilized (Chong et al. 2013). Two meta-analyses also demonstrated no benefit when silicone stenting is added in traditional or external DCR surgeries (Feng et al. 2011; Gu and Cao 2011). The use of silicone stenting varies by surgeon preference and clinical scenario.

Intubation Devices

Silicone is currently the material of choice for intubation devices as silicone has proved to be inert, flexible, well tolerated, and extremely durable.

Intubation devices can be divided broadly into monocanalicular or bicanalicular categories. Monocanalicular tubes traverse either the upper or lower canaliculus, whereas bicanalicular tubes enter into both the upper and lower canaliculi. Bicanalicular tubes form a continuous loop in the medial palpebral fissure with both ends of the tube in the nasolacrimal system. Monocanalicular tubes have one end at the



Silicone Intubation, Fig. 1 Cartoon depicting Mini-Monoka monocanalicular intubation device (*gray*) traversing the lower canaliculus

punctum – usually a blunted or bulbed end – and the other end in the nasolacrimal system.

The Mini-Monoka silicone stent is an example of a commonly used monocanalicular intubation device (Fig. 1). The Mini-Monoka is advanced through the punctum into the canaliculus and terminates in the nasolacrimal system. At the proximal end of the tube, a plug is available in different sizes to prevent the tube from dislocating further into the nasolacrimal system. The tube can be easily removed by grasping the bulb end in the puncta and pulling the tube out through the lid.

The Crawford tube is an example of a bicanalicular intubation device utilizing metal probes with round- or olive-shaped tips. The metal probes are used to thread through the lacrimal system both in the upper and lower canaliculi and are then retrieved in the nose using a Crawford hook. The probes are removed, and the silicone tubes are tied, sutured to the nasal sidewall, or left free to hang in the nose.

Complications

Intraoperative complications of silicone stents include false passage and tube breakage during intubation. Lacrimal probing is essentially a blind procedure guided entirely by feel and mastery of nasolacrimal anatomy. Creation of false passage may lead to scarring and/or further stenosis of the lacrimal passage (Schaefer 2014).

Tube prolapse is probably the most common complication reported in the use of silicone tubes. Lower lid laxity, low knot position, and younger or less compliant patient all increase risk for tube prolapse. Corneal and conjunctival irritation, punctal erosion, and generalized patient discomfort may all result from tube prolapse. Artificial tears and ointment can alleviate some discomfort. Prolapse often results in earlier tube removal, though multiple studies have suggested that the duration the tube remains in place does not correlate with outcome. Occasionally, on postoperative exam, tubes are no longer present on visual inspection of the punctum. Nasal endoscopy should be performed with tube loss given potential for foreign body retained in the nasolacrimal system.

Additional postoperative complications of silicone intubation include erosion or cheese wiring of the tube and granuloma formation. Chronic rubbing and irritation or tubes inserted with inappropriate distribution of tension are hypothesized to cause erosion. Tubes should be removed when persistent erosion is observed though this must be balanced with potential for canalicular stenosis (Korn and Kikkawa 2016). Pyogenic granulomas are initially treated with topical steroids. With failure of topical therapy, granulomas can be removed surgically.

Cross-References

- ▶ Trauma, Canalicular
- ▶ Trauma, Lacrimal Sac and Nasolacrimal Duct

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Silicone IOL

► Silicone Intraocular Lens

Silicone Oil

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Definition

Silicone oil in ophthalmology is used in vitreoretinal surgery where a long tamponade is needed to maintain the adhesion between retina and retinal pigment epithelium for a long period. It is a sterile, highly purified long-chain polydimethylsiloxane.

Its viscosity is measured in centistokes (cs). It ranges from 1,000 to 5,000 cs.

Surgeons prefer silicone oil tamponade due to its extended effect that can remain in the eye for months or years. In addition, it is the best option for eyes with multiple breaks or large retinotomies. There are no restrictions on air travel. Furthermore, it provides a better tamponade in eyes with hypotony.

Indication

The indication for use of silicone oil is related to the factors around the retinal surgery, like complicated retinal detachment, trauma, giant retinal tear, retinal detachment related to viral retinitis, patients with severe proliferative diabetic retinopathy, and tractional retinal detachment. Also, it is indicated in patients that have to fly or that are not cooperative for head positioning like children.

Contraindication

Use of silicone oil is contraindicated in pseudophakic patients with a silicone intraocular lens, due to chemical interaction of silicon oil and lens creating a thick coating with droplet formation on the lens surface.

Techniques and Principles

Silicone oil injection: After completing vitrectomy for retinal detachment repair and immediately after completing fluid-air exchange, the silicone oil is injected into the vitreous cavity through one of the vitrectomy surgery ports; it can be injected through a 23G port but often the sclerotomy is enlarged to 20G. The silicone oil is injected under direct visualization with the wide-angle view system. The air infusion pressure is lowered to 10 mmHg. When the silicone oil reaches the level of the infusion cannula, it is disconnected from the system to prevent sudden elevation of intraocular pressure, thus permitting the remaining air to exit trough the infusion cannula. At this point, the aim is to achieve a full vitreous cavity with a normal intraocular pressure. After completing the silicone oil injection, careful closure or suturing of sclerotomies is performed.

Silicone oil removal: A standard three-port vitrectomy is commonly used to remove silicone oil, with active suction from a 23G or 25G port using 10 ml syringe with a silicone cannula. In case of heavy fluorinated silicone, a larger silicone tube connected to the aspiration system is used to aspire above the optic nerve head. A common practice is to perform one or two fluid-air

exchanges to wash out every remaining bubble of silicone. At the end of the procedure, air or balanced salt solution can be left in the vitreous cavity.

Outcome

After removal of silicone oil, eyes with attached retinas generally showed improvement in visual acuity.

Complications

Cataract formation is one of the most common complications after silicone oil tamponade of the retina. This complication usually is detected within 4–8 months.

Elevation of intraocular pressure is common due to different types of mechanisms. After migration of emulsified silicon bubbles into the anterior chamber, damage can occur to the trabecular meshwork. Also elevation of IOP occurs in several instances. Elevation can be secondary to overfill of silicone oil. It can be due to pupillary block in aphakic eyes blocking the passage of aqueous humor to anterior chamber with aqueous misdirection, shallow anterior chamber, and closed angle.

Band keratopathy is another complication of the use of silicone oil. It can be present after migration of silicone oil to anterior chamber but not necessary always.

Macular pucker is observed within 6 months and occurs in 4–11% of eyes after successful conventional surgery for retinal detachment without PVR. Using data from the Silicone Study, we found in our center, that the 6-month point prevalence rate of postoperative macular pucker was 15%.

Recurrent retinal detachment and missed retinal breaks give raise to recurrent retina detachment.

Cross-References

- ▶ Pars Plana Vitrectomy
- ▶ Retinal Detachment

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Silicone Oil Tamponade

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Synonyms

Polydimethylsiloxane

Definition

Fluid of lower density than water which is used in vitreoretinal surgery for various indications as vitreous tamponade

Epidemiology

Silicone oil as vitreous tamponade is used worldwide, especially for retinal detachment with proliferative vitreoretinopathy (PVR), severe diabetic retinopathy, giant tears, or severe trauma.

History

Silicone oil as vitreoretinal tamponade was introduced by Cibis in 1962, before pars plana vitrectomy was established. By injection of silicone oil into the vitreous cavity along with transscleral drainage of subretinal fluid, the hydraulic forced allowed reattachment of the retina (Cibis et al. 1962).

When pars plana vitrectomy was introduced in 1971 and further developed, Haut established the combination of pars plana vitrectomy and silicone oil endotamponade.

There was a discussion on possible toxicity of silicone oil that led to temporary withdrawal of FDA admission in 1966. This possible toxic effect was mainly due to short-chained silicone oils (Capone and Aaberg 1995).

Nowadays, purified long-chained silicone oil (>2,4 kDa) shows no toxicity, and there are various reports on long-term tamponade by silicone oil.

Clinical Features

There are several types of different silicone oil used for endotamponade. The most common are 1000 cst and 5000 cst silicone oil, with Stoke being the unit for kinetic viscosity (cst = 1 mm^2/s)

Additionally, heavy silicone oil with a higher-than-water-density is becoming more popular to treat inferior retinal detachment with PVR.

As silicone oil is not absorbed, it has to be removed during a second surgery.

Complications of silicone oil used as endotamponade are emulsifications which occur during long-term tamponade and cause secondary glaucoma. These emulsifications may also be found in optic nerve structures in some cases.

Additionally, silicone oil may induce endothelial cell loss of the cornea when in contact with corneal endothelium. Therefore, displacement of silicone oil into the anterior chamber has to be avoided; otherwise, corneal edema and secondary corneal ulceration may occur.

Tests

Biocompatibility of silicone oil has been shown in numerous studies. One study mentioned vacuoles of silicone oil in retinal tissue. These vacuoles are nowadays believed to be preparation artifacts.

Differential Diagnosis

"Silicone" must not be confused with "silicon," which is the chemical element with the symbol Si.

Etiology

The term "silicone oil" refers to polydimethylsiloxane. There are short-chained oils that may induce phagocytosis and inflammation. Therefore, nowadays only purified long-chained silicone oil is used.

Treatment

In ophthalmology, there are several indications for endotamponade with silicone oil, the most prominent being retinal detachment with PVR, severe diabetic retinopathy, rubeosis iridis, and severe trauma.

Cross-References

▶ Diabetic Retinopathy
▶ Retinal Detachment
▶ Silicone Oil

References

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Silicone, Uses in Ophthalmology

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Synonyms

Polyorganosiloxane; Polysiloxane

Definition

A broad family of synthetic organosiloxane polymers containing a repeating silicon-oxygen backbone with organic side groups attached via carbon-silicon bonds. Depending on their structure, silicons are classified as liquids, gels, and elastomers.

Epidemiology

Soft contact lenses, intraocular lenses, and oil tamponades made of silicone are produced and used throughout the world.

History

At the beginning of the twentieth century, chemist F. S. Kipping experimented with the element silicon and its compounds. Thereby, he discovered substances similar to resin and named them "silicon ketones." In 1940, E. G. Rochow and R. Mueller found a way for industrial fabrication of methylchlorosilanes. Quickly after commercial availability of silicone materials in 1946, methylchlorosilanes were described to treat glassware to prevent blood from clotting. At the same time, F. Lahey implanted a silicone elastomer tube for duct repair in biliary surgery. Since these pioneers, interest for silicones in medical applications has remained because of their recognized biocompatibility. In 1962, silicone oil was introduced into vitreoretinal surgery as an endotamponade by P. A. Cibis (Cibis et al. 1962). As an intraocular lenses material, silicone has been used since the early 1980s with Food and Drug Administration (FDA) approval obtained in 1990. The first silicone-hydrogel soft contact lens was launched in 1999 onto the market. This new material encapsulated the benefits of silicone with the extremely high oxygen permeability with the comfort and clinical performance of the conventional hydrogels which had been used for soft contact lenses the previous 30 years.

Clinical Features

Silicones show good electrical insulation; thermal stability; excellent resistance to oxygen, ozone, and UV light; low chemical reactivity; low toxicity; and high gas permeability and do not stick. In medical devices and pharmaceutical applications, silicones are used because of their biocompatibility in a wide variety of physical forms. These forms range from volatile and low oligomers to high molecular weight polymers with viscosities from 0.65 to 20 $\times$ 106 cSt to viscoelastic compounds and cross-linked elastomers.

Tests

Biocompatibility of silicone materials has been shown in numerous studies.

Differential Diagnosis

"Silicone" must not be confused with "silicon," which is the chemical element with the symbol Si.

Etiology

The term "silicone" refers to "silicon ketone" and was coined by F. S. Kipping to describe polydiphenylsiloxane by analogy of its formula Ph_2SiO.

Treatment

In ophthalmology, most important silicon products are soft contact lenses, intraocular lenses, endotamponades for vitreoretinal surgery, and punctum plugs.

Cross-References

- ▶ Contact Lens-Induced Conjunctivitis
- ▶ Intraocular Lens
- ▶ Silicone Intraocular Lens
- ▶ Silicone Oil

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Silk-Screen Retinopathy

- ▶ Cellophane Maculopathy

Simple Anisocoria

- ▶ Physiologic Anisocoria

Simple Lentigo

- ▶ Lentigo Simplex (Simple Lentigines)

Simple Rotational Flap

- ▶ Rotational Flap for Eyelid Repair

Single-Photon Emission Computed Tomography

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Definition

Clinical single-photon emission computed tomography (SPECT) is the use of gamma ray-emitting radiopharmaceuticals to produce functional imaging of an organ or tissue of the human body. In SPECT, the selected injectable radioisotope emits a single photon of gamma radiation as it decays. These emitted rays travel outside of the body and are received by the

surrounding detectors which translate the signal into a 2D horizontal, cross-section image. Many of these images are compiled and reconstructed to make a functional 3D image. In SPECT imaging, disease or aberrant structures can be seen as abnormally bright or dark regions within an image (focal deficit of the radiotracer).

In contrast to conventional structural imaging like CT or MR scans, SPECT allows for functional imaging which reveals characteristics such as glucose metabolism, blood flow, and receptor concentrations at different points in the body. However, unlike structural imaging, SPECT alone does not provide sufficient spatial resolution for accurate topographical localization like x-ray-based computed tomography (CT) scanning. Therefore, a SPECT study is typically combined with a matching CT scan (referred to as SPECT/CT) for the purpose of combining functional and anatomical imaging. The result is a combined image with identification of a functional abnormality on SPECT that is correlated with a structural localization on CT.

History

The first gamma-ray scanning device using a calcium tungstate scintillator was developed in 1949 by Cassen et al. Two years later, clinical usage of a commercial-based scanner, based on Cassen's design, was developed by Reed-Curtis. These early gamma scanning devices used only a single detector; however, multi-detector devices started to emerge after the development of the first computer-controlled dual-detector scanner from Kuhl and Edwards at the University of Pennsylvania in 1964. In the following years, commercial industries began to build multi-detector scanners in attempt to improve image quality and resolution in the following years.

Basic Mechanism

A selected radiopharmaceutical is injected into the patient. As the radioisotopes decay, gamma rays are emitted and are first passed through a collimator to filter out indirect rays which, if unfiltered, would result in excess noise in the computed image. The filtered rays deposit their energy into a scintillation crystal that converts the emitted gamma rays into multiple visible light photons which move through the crystal to an arrangement of high-sensitivity photomultiplier tubes (PMTs). After receiving these visible photons, each of the PMTs produces an electrical current proportional to the amount of photons it detects. Computational software collects the inferred points of emission of each photon and translates each to a specific location in a 2D image. Multiple 2D image cross sections are reconstructed to produce a functional 3D image.

Clinical Uses

SPECT may be used for bone analysis studies, brain studies, and myocardial perfusion. In bone SPECT, uniform distribution of the radioisotopes indicates a normal result, while focal uptake might be indicative of an abnormality (e.g., neoplasm). In brain SPECT, abnormalities can be seen as hypoactivity (e.g., hypoperfusion) or hyperactivity in various regions. Myocardial perfusion SPECT utilizes two different radioisotopes, Thallium-201-TiCl and Technetium-99m-sestamibi, and images the heart at rest and at stress, respectively. Abnormalities can be identified by comparing the two studies. Many SPECT studies use various forms of the radioisotope Technetium-99m.

Comparison with PET

The radioisotopes emitting single photons used in SPECT differ from those used in the related nuclear imaging process of positron emission tomography (PET) where positrons emitted from radioisotopes undergo annihilation to produce two gamma photons. Using only a single gamma photon per decay event, SPECT has a lower image resolution than PET. However, SPECT imaging is more widely available and less expensive than PET systems.

Radiopharmaceuticals for SPECT imaging are likewise more affordable, are longer-lived isotopes, and can involve a large variety of isotopes and tracer compounds. However, PET is usually the preferred imaging method in research applications due to its higher resolution (See "► Positron Emission Tomography").

Cross-References

► Helical Computed Tomography
► Positron Emission Tomography

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Sinuses

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Synonyms

Paranasal sinuses

Definition

The paranasal sinuses comprise of the ethmoid sinus, frontal sinus, maxillary sinus, and sphenoid sinus.

Structure

The nasal sinuses are lined with pseudostratified ciliated columnar respiratory epithelium with many goblet cells. They arise from and drain into the nasal cavity. The drainage is facilitated by cilia hairs.

The paranasal sinuses surround the nasal cavity and drain into the nasal cavity. The nasal wall is composed of the superior, middle, and inferior turbinates that appear as bulbous projections into the central space. The turbinates divide the nasal cavity into three air passages: the superior, middle, and inferior meati. These are inferior to each respective turbinate.

The frontal sinus is not seen radiographically until the sixth year of life, and pneumatization is not complete until early adulthood. The frontal sinus empties into the middle meatus. The right and left frontal sinuses are separated by the intersinus septum.

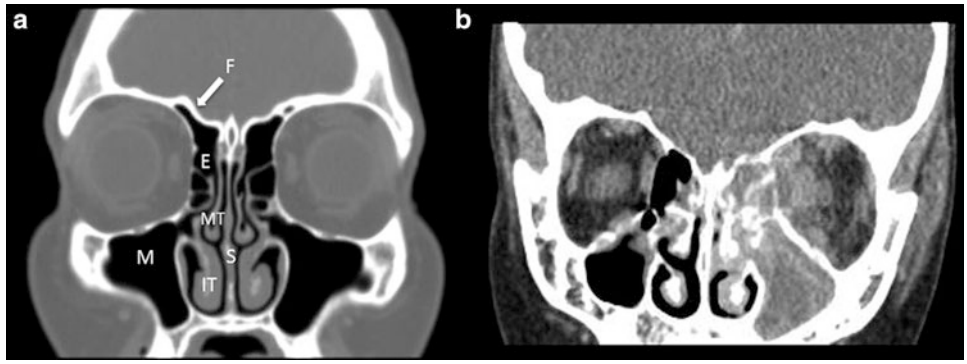
The ethmoid sinus is located between the orbit and the nose. It consists of ethmoid air cells that lie between the medial orbital wall and lateral wall of the nose. They expand in the early years of childhood and can extend into the frontal, lacrimal, and maxillary bones. The anterior and middle air cells drain into the middle meatus; the posterior air cells train in the superior meatus. It is often from the ethmoid sinuses that orbital cellulitis develops.

The sphenoid sinus is the most posterior sinus and is located immediately inferior and medial to the optic canal and internal carotid artery. It is embedded into the clivus. The sinus develops through childhood reaching its full size at puberty. It drains into the sphenoethmoidal recess of each nasal fossa, which lies just lateral to the nasal septum.

The maxillary sinus is the largest of the paranasal sinuses and forms the floor of each orbit. The infraorbital nerve and artery travel along the roof of the sinus and floor of the orbit from the inferior orbital fissure. The sinus drains into the middle meatus of the nose through the maxillary ostium (Fig. 1).

Function

The sinuses function to warm and humidify the air, trap irritants, lighten the weight of the skull, act as a resonating chamber for the voice, and



Sinuses, Fig. 1 (**a**) CT Sinus demonstrating sinus anatomy. *M* maxillary sinus, *F* frontal sinus, *E* ethmoid sinus, *S* septum, *IT* inferior turbinate, *MT* middle turbinate. (**b**) CT Sinus of a 12-year-old male with severe sinusitis demonstrating dense opacification of the anterior and posterior ethmoid air cells, left greater than right, and complete opacification of the left maxillary sinus. In addition, there is also a medially based small subperiosteal abscess that ultimately required surgical drainage

provide protection for the brain in the case of trauma.

Clinical Relevance

Understanding the anatomy of the sinuses is relevant in ophthalmology as it is through the sinuses that orbital tumors or orbital infections often spread. Pathophysiologic processes of the sinuses that secondarily affect the orbit include sinonasal carcinomas, inverted papillomas, zygomycoses, Wegener granulomatosis, mucoceles, and sinusitis which may cause orbital cellulitis or abscesses. Orbital fractures also usually prolapse into the sinuses.

Bacterial orbital cellulitis is most commonly caused by spread of infection in the ethmoid sinus either into the orbit directly through the lamina papyracea or via the anterior or posterior ethmoidal vessels. The frontal, sphenoid, and maxillary sinuses are less often the culprit. Orbital complications of paranasal sinusitis can include superior ophthalmic vein thrombosis, cavernous sinus thrombosis, and blindness, although these are rare.

Mucoceles can develop in the frontal sinus when there is obstruction of the sinus drainage. This can lead to displacement of the orbital contents inferiorly and laterally over time.

Inferior orbital floor fractures, or blowout fractures, cause prolapse of orbital tissues into the maxillary sinus. This is why it is recommended not to blow one's nose if there is an inferior floor fracture to avoid causing orbital emphysema. The infraorbital nerve can also be injured in these fractures causing hypesthesia of the cheek and upper gingiva.

Given how close the sphenoid sinus is to the optic nerve, sphenoid sinusitis may cause damage to the optic nerve.

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Sipple Syndrome

▶ Sipple-Gorlin Syndrome, Enlarged Corneal Nerves

Sipple-Gorlin Syndrome, Enlarged Corneal Nerves

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Synonyms

Multiple endocrine neoplasia (MEN) 2B; Sipple syndrome

Definition

Enlarged corneal nerves are stromal corneal nerves visible at the slit lamp that appear thickened, beaded, or to have perineural inflammation. Sipple-Gorlin syndrome (MEN 2B) is an autosomal dominant disease characterized by medullary carcinoma of the thyroid gland, pheochromocytoma, and mucosal neuromas. Ophthalmic findings in MEN 2B syndrome can include enlarged corneal nerves, conjunctival and eyelid neuromas, thickened upper eyelids with mild ptosis and eversion of the eyelid margins, and keratoconjunctivitis sicca. Other typical features of MEN 2B include marfanoid habitus and a long history of diarrhea and/or constipation (Eter et al. 2001; Kim and Dohlman 2001; Parker et al. 2004).

Etiology

Enlarged corneal nerves are most importantly associated with MEN 2B (Sipple-Gorlin syndrome). MEN 2B is inherited in an autosomal dominant pattern and is associated with high mortality from metastatic thyroid carcinoma, with reported 5-year survival rates of 35%. Up to 60% of cases of MEN 2B are associated with de novo mutations (Eter et al. 2001). Mutations in the *RET* proto-oncogene on chromosome 10 are associated with MEN 2B. Familial medullary thyroid cancer patients, who have medullary thyroid cancer but do not have pheochromocytomas, also often have enlarged corneal nerves. Patients with MEN 2A have occasionally also been noted to exhibit mildly enlarged corneal nerves (Kim and Dohlman 2001).

The prominent corneal nerves in MEN 2B have been found to consist of an increased number of nonmyelinated axons in close association with Schwann cells (Spector et al. 1981).

Other diseases associated with enlarged corneal nerves include Refsum syndrome (phytanic acid storage disease), leprosy (Hansen disease), familial dysautonomia (Riley-Day syndrome), neurofibromatosis type 1, and *Acanthamoeba* keratitis (Kim and Dohlman 2001). Corneal nerves may be more visible but not necessarily enlarged in keratoconus, ichthyosis, Fuchs endothelial dystrophy, posterior polymorphous corneal dystrophy, corneal edema, herpes simplex, herpes zoster, and congenital glaucoma (Eter et al. 2001).

Occurrence

Enlarged corneal nerves are a ubiquitous manifestation of MEN 2B. All patients described in the literature with MEN 2B have displayed enlarged corneal nerves. In MEN 2B, the enlarged corneal nerves are usually present in the first decade and have been detected as early as 2 years of age. Seven of 11 members of a family with familial medullary thyroid cancer, without the other manifestations of MEN 2B, were found to have enlarged corneal nerves. Enlarged corneal nerves are less often a manifestation of other conditions in an otherwise normal-looking cornea.

Classification

In MEN 2A medullary thyroid cancer occurs with pheochromocytoma and hyperparathyroidism. In MEN 2B medullary thyroid cancer occurs with pheochromocytoma and hyperparathyroidism and in addition, mucosal neuromas, marfanoid body habitus, gastrointestinal ganglioneuromatosis, and ophthalmic abnormalities.

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Sixth Cranial Nerve

► Cranial Nerve VI (Abducens Nerve)

Sixth Nerve Palsies

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Synonyms

Abducens nerve palsy; Cranial sixth nerve palsy; Lateral rectus palsy; Sixth nerve palsy

Definition

Abducens nerve palsy is dysfunction of the sixth cranial nerve which provides the motor innervations to the ipsilateral lateral rectus muscle. It has a long subarachnoid course and is thus susceptible to dysfunction from increased intracranial pressure. The sixth nerve nucleus is located ventral to the floor of the fourth ventricle and lateral to the medial longitudinal fasciculus (MLF) at the level of the pons. The nucleus provides innervation via the MLF to the contralateral third nerve nucleus and medial rectus muscle to coordinate horizontal gaze. The fascicle of the sixth nerve travels ventrally and exits the pons into the subarachnoid space then proceeds rostrally along the clivus and turns to enter the substance of the cavernous sinus lateral to the internal carotid artery but medial to the dural wall of the cavernous sinus. From the cavernous sinus, the sixth nerve enters the orbit via the superior orbital fissure to innervate its target extraocular muscle, the lateral rectus muscle.

Etiology

The most common cause of an isolated sixth nerve palsy in adults over age 50 years is ischemic. In one population-based study, the causes of sixth nerve palsy were as follows: hypertension alone (19%), concomitant hypertension and diabetes (12%), trauma (12%), multiple sclerosis (7%), neoplasm (5%), diabetes alone (4%), cerebrovascular accident (4%), post-neurosurgery (3%), aneurysm (2%), and other miscellaneous causes (8%). Sixth nerve palsy was the presenting sign in only one case of neoplasm and in three aneurysms. In contrast to adults, neoplasm is one of the leading causes of sixth nerve palsy in children.

Given the anatomical position of the sixth cranial nerve within the substance of the cavernous sinus, it is believed to be more vulnerable than other cranial nerves which are relatively more protected in the dural wall of the cavernous sinus. In addition, intracavernous pathology (e.g., carotid aneurysm, meningioma, carotid-cavernous fistula) can present with sixth nerve palsy with or without concurrent Horner's syndrome or other ocular motor cranial neuropathies or trigeminal neuropathy. As noted previously, a unilateral or bilateral sixth nerve palsy can also present as a non-localizing sign of increased intracranial pressure (e.g., idiopathic intracranial hypertension). In addition, an isolated sixth

nerve palsy can also occur due to clivus lesions (e.g., chordoma, meningioma). Thus, an isolated and especially chronic or progressive sixth nerve palsy can be a harbinger of underlying neoplasm without other neurologic signs or symptoms. Despite modern neuroimaging techniques, however, up to 25% of cases remain of undetermined etiology. Serial imaging might still be necessary in progressive or chronic cases with special attention to the cavernous sinus or clivus.

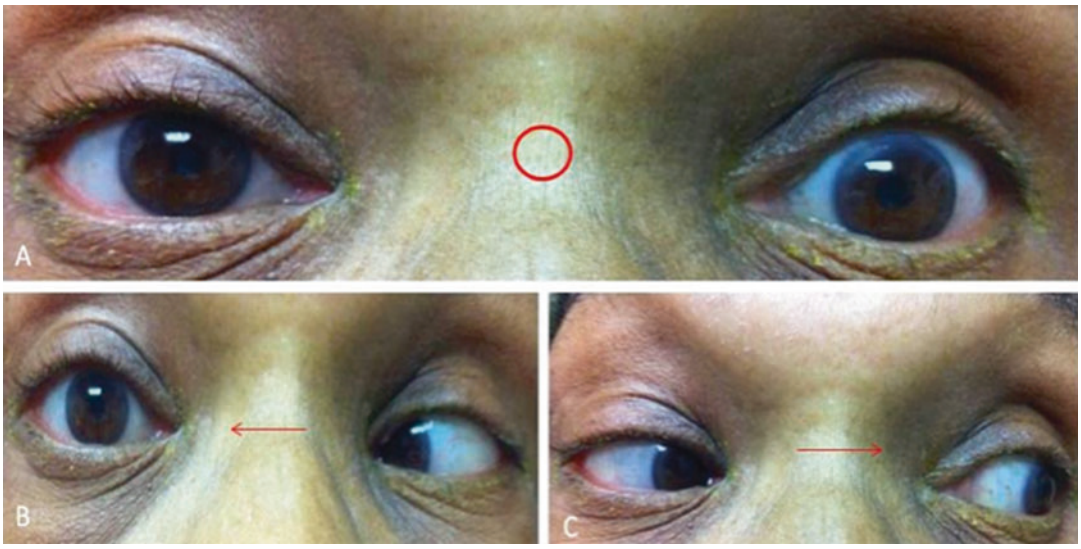
Clinical Presentation

Patient with a sixth nerve palsy usually present with binocular, horizontal diplopia that is worse with gaze in the direction of action of the impaired lateral rectus muscle (see Fig. 1). Extraocular muscle examination usually shows an esotropia (ET) in the primary position that worsens (laterally incomitant ET) with gaze in the direction of the affected lateral rectus muscle. Thus, the patient may present with an anomalous face turn to minimize the diplopia by looking away from the affected lateral rectus muscle. In addition to the diplopia, the patient may have other symptoms (e.g., headache, facial numbness) or signs (e.g., ptosis, facial nerve palsy, trigeminal numbness, anisocoria) depending on the localization of the sixth cranial nerve lesion. Thus, one of the critical components of the evaluation of a sixth nerve palsy is to insure that it is truly neurologically isolated or conversely to anatomically localize the lesion based on the accompanying symptoms or signs.

Diagnostics

The evaluation for an isolated and presumed vasculopathic sixth nerve palsy is controversial but many sources suggest that watchful waiting for improvement is appropriate for up to 2–3 months when vasculopathic risk factors are present. However neuroimaging (preferably contrast-enhanced MRI of the brain following the course of the sixth nerve) is indicated if the sixth nerve palsy is not neurologically isolated and is progressive or if the presumed vasculopathic sixth nerve palsy fails to improve or worsens after the initial observation. Atrophy of the lateral rectus muscle is seen in denervation atrophy and can be a radiographic sign of chronic and long-standing sixth nerve palsy.

An emergent head CT may be preferred over MRI in some settings especially when there is a history of trauma or if evaluation of orbital disease, sinus, bone, acute bleeding, or foreign body



Sixth Nerve Palsies, Fig. 1 Patient with left sixth nerve palsy with esotropia in the primary position that worsens in the direction of affected lateral rectus muscle.

is required. However, typically in nontraumatic cases, if there is no contraindication to MRI, then a cranial MRI with contrast is the imaging modality of choice for sixth nerve palsy.

Other diagnostic testing obviously could be considered depending on the suspected etiology. For example, an MRV may be necessary if increased intracranial pressure due to possible cortical venous sinus thrombosis is suspected (e.g., sixth nerve palsy with papilledema). A lumbar puncture might also be indicated if the neuroimaging is negative or suggestive of increased intracranial pressure or meningeal disease. Laboratory studies may be considered depending on the clinical presentation including complete blood cell (CBC) count, erythrocyte sedimentation rate, and/or C-reactive protein (in elderly patients suspected of having giant cell arteritis), rapid plasma reagin (RPR) test or fluorescent treponemal antibody-absorption test (FTA-ABS) for syphilis, or Lyme titer. Because thyroid eye disease could mimic the abduction deficit and esotropia of sixth nerve palsy, thyroid function tests and orbital imaging (e.g., orbital ultrasound or CT of the orbit) might be useful. Myasthenia gravis (MG) can mimic any painless, pupil-spared ophthalmoplegia including sixth nerve palsy, and evaluation for MG might include anti-acetylcholine receptor antibodies, edrophonium (Tensilon) or ice testing, neurologic consultation, etc (Patel et al. 2004; Lee et al. 2009; Gonçalves et al. 2002).

Differential Diagnosis

1. Thyroid eye disease (restrictive involvement of the medial rectus muscle)
2. Idiopathic intracranial hypertension (non-localizing sixth nerve palsy)
3. Giant cell arteritis (myogenic or neurogenic ischemic)
4. Myasthenia gravis
5. Duane syndrome
6. Convergence spasm (papillary miosis, variable deviation)

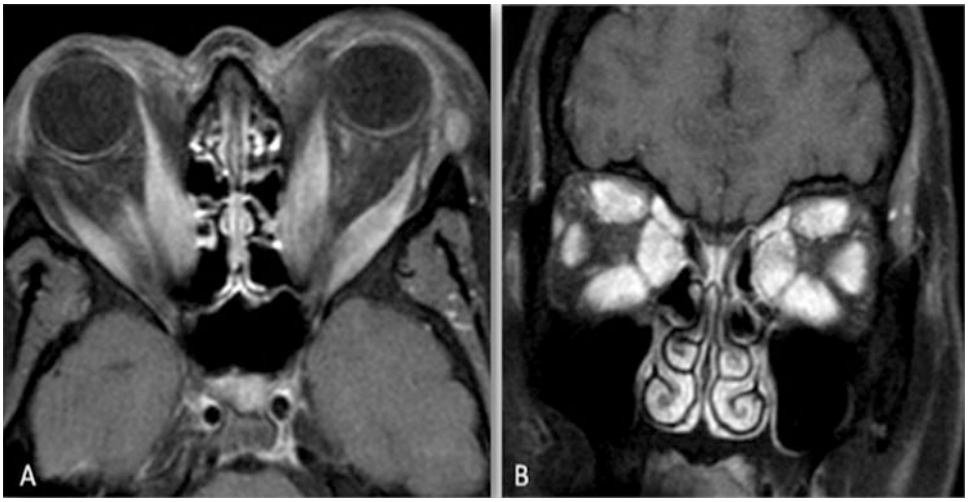
Thyroid Eye Disease (TED)

A restrictive myopathy of the medial rectus muscle (rather than a paretic sixth nerve process) can produce an incomitant esotropia, an abduction deficit, and a deviation worse in the direction of the presumed paretic lateral rectus muscle that can mimic a sixth nerve palsy. TED is an autoimmune disorder that causes an inflammatory enlargement and secondary fibrotic contraction of the extraocular muscles. Although the inferior rectus is the most commonly affected muscle (resulting in restriction on upgaze and hypotropia), the medial rectus is the second most affected muscle in TED and thus can present with abduction deficit resembling a sixth nerve palsy. Restrictive myopathy (TED) can be differentiated from an acute isolated paretic sixth nerve palsy with forced duction testing or saccadic testing (restrictive saccade versus slowed, paretic saccade). Patients with a presumed sixth nerve palsy especially with a history of autoimmune thyroid disease should be evaluated for the presence or absence of other signs of TED (e.g., lid retraction, lid lag, chemosis, conjunctival injection, proptosis, compressive optic neuropathy, etc.)

TED usually results in bilateral symmetric enlargement of multiple extraocular muscles with sparing of the tendon that can be seen radiographically on CT, MR, or ultrasound (see Fig. 2) of the orbits. Although cranial MRI with contrast is the imaging study of choice for unexplained sixth nerve palsy, an orbital study could be added to the MR scan if there is some doubt about potential TED mimicking sixth nerve palsy.

Idiopathic Intracranial Hypertension (IIH), Also Known as Pseudotumor Cerebri (PTC)

An isolated unilateral or bilateral sixth nerve palsy can be a non-localizing sign of increased intracranial pressure (ICP) and occurs in approximately one fourth of cases of IIH. Other associated signs and symptoms of increased ICP may include headache, transient visual obscurations, or tinnitus. Patients with suspected increased ICP should be evaluated for papilledema, rarely choroidal folds, and nerve fiber visual field defects on formal visual field testing. Radiographic signs of increased ICP might include an empty sella, flatting of the posterior globe, and visible cerebrospinal fluid within the optic nerve sheath. An elevated opening pressure with normal cerebrospinal fluid content in the setting of normal neuroimaging (except for signs of



Sixth Nerve Palsies, Fig. 2 Thyroid eye disease with bilateral enlargement of multiple extraocular muscles.

elevated ICP) is diagnostic of IIH and is a common cause of sixth nerve palsy in adults with papilledema (Quattrone et al. 2006).

Giant Cell Arteritis (GCA)

Although sixth nerve palsy is a rare presentation of GCA, other signs and symptoms of GCA (e.g., headache, jaw pain, visual loss) should be sought in elderly patients with a sixth nerve palsy. Stat serum ESR and CRP, empiric steroid therapy, and a temporal artery biopsy may be necessary.

Myasthenia Gravis (MG)

MG is an autoimmune neuromuscular junction disorder that can produce any pattern of pupil-spared, nonproptotic ophthalmoplegia and can mimic a sixth nerve palsy. Variability and fatigability are the key differentiating symptoms of myasthenia gravis. Other common symptoms (e.g., ptosis, generalized weakness, difficult breathing) and signs (variable ptosis, orbicularis weakness, the Cogan lid twitch sign, enhancement of ptosis) of MG should be evaluated. Patients with suspected MG might require laboratory or other testing for MG.

Therapy

The vasculopathic, isolated sixth nerve palsy in adults typically resolves over time, and recovery is often completed within 3–6 months. Other sixth nerve palsies may improve over time depending on etiology (e.g., postviral, posttraumatic, demyelinating, or idiopathic often improve). For vasculopathic patients, control of the underlying vasculopathic risk factors (e.g., hypertension, diabetes, hyperlipidemia), lifestyle modifications (e.g., weight loss, exercise, smoking cessation), and perhaps a daily aspirin (if no contraindication) are recommended. Prism and patching therapy are the first-line conservative treatments for symptomatic diplopia. *Botulinum* toxin injection could be considered as temporizing measure especially for traumatic sixth nerve palsy as relaxing the medial rectus may allow the lateral rectus time to better recover function. Strabismus surgery is generally reserved for patients who fail, are intolerant to, or noncompliance with patching or initial prism therapy and who have stable ocular deviations.

Prognosis

The majority of idiopathic sixth cranial nerve palsies resolve within 3 months, with vasculopathic sixth nerve palsy more likely to resolve (up to 86%). Sixth nerve palsy however depending on etiology may recur in up to 1/3 of patients, and these patients may require repeat diagnostic evaluations. Patients with progression, bilateral involvement, or lack of recovery should undergo further evaluation including

neuroimaging. Spontaneous recovery within days would be atypical but can be seen in myasthenia gravis or in some mimickers of sixth nerve palsy (e.g., convergence spasm). Recurrent isolated vasculopathic sixth nerve palsy is uncommon but has been reported, and in diabetics recurrent sequential ocular motor cranial mononeuropathies are not uncommon. Multiple simultaneous or rapidly sequential cranial neuropathies however are atypical and should prompt further evaluation for additional diagnoses (Sanders et al. 2002).

Epidemiology

Sixth nerve palsy is the most common ocular motor palsy (representing up to 40–50% of ocular motor neuropathy). The annual incidence of sixth nerve palsy may be up to 11.3 per 100,000 and can affect all age groups, either gender, and any race. The etiology will vary in part depending on the age with ischemic etiologies being more common in older populations and congenital and postviral causes more prevalent in children.

Cross-References

- ▶ Giant Cell Arteritis
- ▶ Idiopathic Intracranial Hypertension
- ▶ Myasthenia Gravis, Overview
- ▶ Thyroid Eye Disease

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Sixth Nerve Palsy

▶ Sixth Nerve Palsies

Skew Deviation

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Synonyms

Hertwig-Magendie sign

Definition

Skew deviation is a vertical deviation that is caused by a lesion to the brainstem, cerebellum, or vestibular system (Wong 2010). The injury can be uni- or bilateral in nature and will result in a misalignment of the vertical axis. There may also be a compensatory head tilt (i.e., the ocular tilt reaction) and torsion (typically bilateral and toward the hypotropic eye) (Brodsky et al. 2006).

Etiology

Skew deviation is primarily seen in older patients who have suffered a stroke that affects the brainstem, but other lesions in the posterior fossa may produce skew (e.g., multiple sclerosis, tumor, trauma, abscess, hemorrhage, or surgical complications) (Brodsky et al. 2006). Rarely, the skew deviation can also come from an acute unilateral vestibular lesion (Brodsky et al. 2006).

Clinical Presentation

Skew deviation often presents as part of the clinical triad including the vertical deviation (typically not localizing to any one extraocular muscle or ocular motor cranial nerve distribution), ocular torsion, and head tilt (Wong 2010). These hallmark signs can be accompanied by torticollis and subjective visual vertical (Brodsky et al. 2006).

Diagnostics

Skew deviation shares many common features with other conditions, and so it is necessary to conduct thorough testing to make the proper diagnosis. Using the double Maddox rod test, a point source of light appears as two red or white (depending on the color of the rod) horizontal streaks (Parulekar et al. 2008). If one or both horizontal streaks were perceived as slanted, the subject is then instructed to rotate the orientation of the rods until the streak(s) becomes parallel horizontally (Parulekar et al. 2008). Ocular torsion and vertical misalignment that decrease from the upright position to the supine position may also indicate skew deviation, whereas torsion and vertical misalignment that do not change significantly between positions are more consistent with trochlear nerve palsy (Parulekar et al. 2008).

Next, the magnitude of vertical strabismus can be measured using the prism and alternate cover test. To properly conduct this test, the patient must not adopt their usual tilted head posture and must sit straight up with their chin parallel to the ground. Prisms of increasing power are then placed over the deviated eye while the cover alternates between the eyes (Parulekar et al. 2008). The highest prism strength when no refixation movement occurred is then recorded.

Differential Diagnosis

(a) Superior oblique palsy
(b) Inferior oblique palsy
(c) Superior division third nerve palsy
(d) Third nerve palsy
(e) Trochlear nerve palsy

Prophylaxis

Therapy

The treatment of skew deviation is directed against the etiology (Brodsky et al. 2006). Some effective treatments for symptomatic diplopia include patching, prisms, botulinum toxin, and vertical rectus muscle recession (Brodsky et al. 2006).

Prognosis

Prognosis for recovery is viable for patients with skew deviation. Seventy percent of patients will recover with a median time of 7.5 months depending on the underlying etiology (Borruat et al. 1998). Surgery should be postponed at least 12 months (Borruat et al. 1998).

Epidemiology

The prevalence of skew deviation depends on the etiology and may occur in any age, or either gender, and may affect any race.

Cross-References

▶ Alternating Skew Deviation
▶ Fourth Nerve Palsy
▶ Third Nerve Palsy

References

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Skin

► Epidermis

Skin Peeling Conditions

► Desquamating Skin Conditions

Skin Tag

► Squamous Cell Papillomas of Eyelid

SLK

► Superior Limbic Keratoconjunctivitis

Sloan Letters

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Synonyms

Sloan optotypes

Definition

A set of standardized sans serif letter optotypes introduced by Louise Sloan (1959). The ten letters (C, D, H, K, N, O, R, S, V, and Z) cover a grid of 5 × 5 (based on the stroke width of the optotypes) and are of similar difficulty to be recognized. The Sloan letter "C" is identical to the Landolt ring. Nowadays, Sloan letters are the standard optotypes in many tests for measuring visual function such as the ► ETDRS chart and the ► Pelli-Robson chart.

Cross-References

► ETDRS Chart
► Minimum Angle of Resolution/Recognition (MAR)
► Pelli-Robson Chart

Reference

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Sloan Optotypes

► Sloan Letters

Snap Test

► Snapback Test

Snapback Test

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Synonyms

Snap test

Definition

The snapback test is a diagnostic procedure utilized in the assessment of eyelid tone and severity of horizontal eyelid laxity.

Purpose

The snapback test is an important part of the preoperative evaluation of involutional eyelid malposition. The ability to identify the severity of eyelid malposition aids in the selection of a surgical repair procedure suitable for each individual. The snapback test may also help in the differentiation of various causes of eyelid malposition (Bartley 1995). Involutional entropion is usually associated with eyelid laxity, while eyelid malposition secondary to cicatricial changes occurs due to eyelid rotation from inflammatory scarring of the eyelid. Fibrous scar tissue increases resistance to traction, which correspondingly increases the difficulty with pulling the eyelid away from the globe in the snapback test, compared to increased ease in cases of involutional entropion.

Principle

The underlying principle of the snapback test is based upon the intrinsic elastic properties of normal tissue. The lower eyelid spans the medial and lateral canthi, and apposition to the globe is normally conferred through the normal tone and elasticity of the eyelid. A decrease in elastic fibers with ultrastructural abnormalities and an overexpression of elastin-degrading enzymes with age results in loss of eyelid tone, and elasticity in involutional ectropion and entropion results in eyelid malposition (Nagi et al. 2011).

Procedure

1. Pull the lower eyelid down and away from the globe for 2–3 s before releasing the eyelid.
2. Assess the time it takes for the eyelid to return to its original position, or the new resting position if the eyelid does not return to its original position. This should be completed without the patient blinking.

Grades

0. Returns to original position immediately
1. Returns to original position in 2–3 s
2. Returns to original position in 4–5 s
3. Returns to original position in >5 s
4. Does not return to original position, remains in a position of ectropion

Indication

Clinical and preoperative evaluation of eyelid laxity and eyelid tone in involutional eyelid malposition.

Contraindication

The snapback test is a simple, noninvasive, and low-risk diagnostic test that is easily incorporated into the clinical examination of the patient with involutional eyelid malposition. Nevertheless, the test should only be performed in patients who have indicated consent to the procedure. The test is contraindicated in cases when pressure around the periocular area should be avoided or when the integrity of the eyelid tissue is compromised. Non-exhaustive examples of such situations include eyelid or periocular trauma and suspicion for globe rupture.

Advantage/Disadvantage

Advantage

The snapback test is simple, easy to learn, and cost-effective and provides a quick and relatively reliable clinical assessment of eyelid malposition that helps with the clinical evaluation and preoperative assessment of patients who are suitable surgical candidates.

Disadvantage

The snapback test grossly evaluates for the presence of eyelid laxity but does not specifically localize the region in which laxity is greatest,

which may alter the surgical plan for repair of eyelid malposition. Additional tests such as lateral and medial traction of the eyelid with observation of punctal displacement may aid with localization of eyelid laxity.

Cross-References

► Congenital Entropion

References

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Snellen Acuity

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Synonyms

Snellen ratio

Definition

For a long time, the visual acuity (VA) chart designed by Herman Snellen in 1862 was the reference chart for VA testing. The basis for the construction of the Snellen chart was an angular subtense of 5 arcmin (5′) of letter height and width (which equals an angle of resolution of 1′ because the stroke width of the letter is one fifth of the height). Snellen considered the angle of 1′ as reference, although many healthy subjects are able to recognize smaller angles. Snellen visual acuity is defined by the equation

$$\mathrm{VA} = d/d_s$$

where d is the distance under which the subject the letter and d_S is the distance under which letter height subtends an angle of 5′ (► MAR 1′). For example, if a subject reads a letter row the letters subtend an angle of 5′ at a testing distance of 6 m, the ratio reads 6/6. If another subject just recognizes the letter row where the angles subtend 5′ at a distance of 12 m (or 10′ at 6 m), the ratio would read 6/12. Another form of expressing Snellen acuity is a fraction of $20/d_S$, based on the testing distance of 20 ft. The decimal form of visual acuity (1/MAR) is equal to the result of the Snellen fraction, because Snellen chose 1′ as reference.

Cross-References

► ETDRS Chart
► Minimum Angle of Resolution/Recognition (MAR)
► Sloan Letters

Snellen Ratio

► Snellen Acuity

Social Disease

► Syphilis: Overview

Solar Keratoses

► Actinic (Solar) Keratosis

Solar Keratosis

► Actinic Keratosis

Solar Lentigo

► Lentigo Senile (Liver Spots)

Solid-State Lasers

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Definition

Solid-state laser is the term used for lasers, which have a solid gain medium, instead of liquid or gaseous gain medium. Although laser diodes also have a solid semiconductor-based gain medium, they are not classified as solid-state laser as the mode of operation of these lasers is different from solid-state lasers.

Overview

The very first laser demonstrated by Maiman was a solid-state laser, which used ruby crystal (Cr^{3+}:Al_2O_3) as the gain medium. Soon afterward neodymium-doped yttrium aluminum garnet, Nd:$Y_3Al_5O_{12}$ (Nd:YAG)-based laser was developed which has become one of the most popular solid-state laser. In the past three decades, new gain mediums based on rare earth ions (Er^{3+}, Tm^{3+}, Ho^{3+}, and Yb^{3+}) and transition metal ions (Cr^{3+} and Ti^{3+}) in a variety of host crystals have been discovered. The emission wavelength of the laser depends on the interaction of the electrons in the metal ion with the electrostatic field in the host crystal. A variety of doping ions and host crystals has enabled solid-state lasers, which emit in UV, visible and NIR wavelengths. To further diversify the emission wavelengths many times, the solid-state lasers are used with nonlinear wavelength conversion techniques such as generation of higher harmonics, sum and difference frequency generation, and optical parametric processes. Tunable solid-state lasers have also been developed using intra-cavity techniques such as using gratings or etalons inside the cavity. Titanium-doped sapphire (Ti-sapphire) laser is a widely used tunable solid-state laser with a tuning range from 660 to 986 nm. Most of the tunable solid-state lasers use gain medium with transition metal ions.

Pumping

Traditionally solid-state lasers were pumped using arc or flash lamps; however, this pumping technique leads to low-power efficiency. Also flash lamps have low lifetime and produce a lot of heat. Recently pumping using laser diodes has gained popularity. Such lasers are called diode-pumped solid-state lasers (DPSS) and offer various advantages over traditionally pumped solid-state lasers, which includes compact design, higher lifetime, and very good beam quality.

Operation

Solid-state lasers can operate in pulsed or continuous wave (CW) or quasi-CW mode. Pulsed lasers generally use Xenon flash lamps for pumping. The high peak power intensity in the pulsed lasers is obtained by Q-switching. In Q-switching, the laser resonator is initially disabled, until the population inversion in the gain medium is complete. The cavity is then allowed to resonate for a short interval of time, during which high intensity pulse is emitted by the laser. The output of the pulsed laser is specified in joules of energy per pulse. To calculate the output power, the energy per pulse is to be multiplied by pulse repetition rate per second. It should be noted that although high peak intensity can be achieved in pulsed solid-state lasers, the average power output for these lasers is quite low.

CW solid-state lasers provide higher average power output as they use diode lasers for pumping, which is very efficient. Arc lamps may also be used for pumping, but this approach is now becoming obsolete as the output power is

low. Quasi-CW lasers are pulsed lasers with very high pulse repetition rate (10–100 KHz) such that the laser appears to be CW. Such high repetition rates are achieved by Q-switching though electro-optics in the laser cavity.

Applications in Ophthalmology

Solid-state lasers have been widely used in ophthalmology to precisely cut soft tissue or break it into smaller pieces. Many of the ophthalmic surgeries are now carried out using solid-state lasers. These surgeries include:

- Femtosecond pulsed solid-state lasers in cutting the flap for LASIK surgery, providing a more precise flap creation, thus reducing complications in the surgery. Corneal ablation for refractive correction however is still carried out using excimer laser, which is not a solid-state laser.
- Laser trabeculoplasty, where solid-state laser is used to burn the trabecular meshwork to increase fluid flow. Increased fluid flow leads to a reduction in intraocular pressure in Glaucoma
- Solid-state lasers are widely used in removing the posterior capsule opacification after cataract surgery by performing YAG capsulotomy.
- In the recent times, laser-assisted cataract surgery procedure has been developed where solid-state laser is used to break the cataract. This has made the surgery more predictable and precise.
- Retinal laser photocoagulation procedure is used in diabetic retinopathy patients. A pulsed solid-state laser beam is made incident on the retina. The resulting heat generated from the incident laser light seals or destroys the leaking blood vessels.

Solid-state lasers have revolutionized the way ophthalmic surgeries are carried out, making these surgeries more precise and controlled. Although solid-state lasers have been replaced by the more robust and compact diode lasers in many industrial CW applications, their superior performance in pulsed laser arena still makes them more suitable for medical applications. Many new areas of application have been explored with these lasers for ophthalmic surgeries, and it is expected that these laser will continue to play a crucial role improving the success rate of ophthalmic surgeries.

Cross-References

▶ Cataract Surgery
▶ Corneal Ablation
▶ Diabetic Retinopathy, Proliferative
▶ Excimer Lasers
▶ Photocoagulation
▶ Posterior Capsule Opacification (PCO)
▶ wg-LASIK

Solitary Trichoepithelioma

▶ Trichoepithelioma

Solodelf

▶ Intravitreal Triamcinolone

SOOF Lift

▶ Cheek Elevation, in Eyelid Repair

Spasm of Accommodation

▶ Accommodation, Functional (Nonorganic/Nonphysiologic) Disorders of

Spasm of Eyelids

▶ Benign Essential Blepharospasm: Neuro-ophthalmic Considerations

Spasmus Nutans

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Definition

Spasmus nutans is usually a benign disorder, unaccompanied by neurologic abnormalities, defined by a triad of signs occurring in the first year of life that consists of pendular nystagmus and head nodding, and torticollis (Quiros and Yee 2014). However, the complete triad is not present in all patients (Quiros and Yee 2014).

Clinical Presentation

The nystagmus of spasmus nutans can be vertical, horizontal, or torsional with a frequency of 3–11 Hz and variable amplitude while varying from conjugated, monocular, and dissociated (eyes beat independent of each other) within a few minutes (Tamhankar and Liu 2008). The nystagmus is converted to a larger amplitude, slower, binocularly symmetrical, pendular oscillations with improved vision due to head nodding inducing vestibulo-ocular responses (Tamhankar and Liu 2008). However, the head bobbing occurs less frequently than the nystagmus, and is thus not considered a compensatory action (Lavin 2012).

Diagnostics

The diagnosis is one of exclusion. Diagnostics include careful clinical examination and electronic recordings of eye and head movements to differentiate spasmus nutans from congenital nystagmus (Tamhankar and Liu 2008). The nystagmus frequency is higher and the amplitude more variable in spasmus nutans (Tamhankar and Liu 2008). MRI studies may be warranted to differentiate spasmus nutans from CNS tumors in patients with accompanying visual loss, relative afferent papillary defect, optic atrophy, abnormal growth and development, or older age of onset (Tamhankar and Liu 2008).

Differential Diagnosis

Visual loss in children, intracranial tumors, congenital nystagmus, retinal disorders, spinocerebellar degeneration.

Prognosis

The syndrome typically resolves by age 1–2 years, but electronic eye movement recordings show small-amplitude, intermittent, dissociated pendular nystagmus that may be present until age 5–12 years (Tamhankar and Liu 2008).

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Specular Photomicroscopy

▶ Photomicroscopy, Specular

Sphaerularis Elaiodes

▶ Keratinoid (Spheroidal) Degeneration
▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
▶ Spheroidal Degeneration

Sphenoid Bone

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Structure

The sphenoid bone is a compound bone that forms the base of the cranium and contributes to all walls of the orbit except the floor. It resembles a butterfly and consists of a central median portion, known as the body, which is flanked by a set of two greater and two lesser winglike projections that extend out laterally on either side. The lesser wing of the sphenoid contributes to the orbital roof along with the frontal bone, as well as to the medial wall along with the lacrimal, ethmoid, and maxillary bones. The greater wing of the sphenoid joins the zygomatic bone in forming in the orbit's lateral wall.

At the anterior surface of the sphenoid is the sphenoidal crest, which contributes to the nasal septum and is flanked by the openings of the two sphenoidal air sinuses that comprise the body of the sphenoid. On the most anterior extent of the superior surface of the body is the ethmoidal spine, which articulates with the cribriform plate of the ethmoid. Moving posteriorly on the superior surface, the ethmoidal spine is followed by a smooth surface with a slightly raised midline that creates a groove into which the olfactory bulbs rest. Directly posterior to the olfactory grooves is a transverse ridge that forms the anterior boundary of the chiasmatic groove (optic groove), which ends on either side in the optic foramen. The optic chiasm rests on the chiasmatic groove, and the optic nerve and ophthalmic artery are carried through the optic foramen into the orbital cavity. The optic foramen is the opening to the optic canal, which transmits the optic nerve, ophthalmic artery, and sympathetic fibers into the orbital cavity. The left and right optic canals are oriented 25 mm apart posteriorly and 30 mm apart anteriorly (Black et al. 2012).

Dorsal to the chiasmatic groove is a deep saddle-shaped depression known as the sella turcica that houses the pituitary gland (hypophysis). The anterior boundary of the sella turcica is formed by the two middle clinoid processes; the posterior boundary is formed by the dorsum sellae with two projecting tubercles known as the posterior clinoid processes. On the surface of the dorsum sellae is a notch along which the abducens nerve passes. Directly behind the dorsum sellae is the clivus, which articulates with the occipital bone and supports the pons. The posterior surface of the sphenoid body joins to the occipital bone by a plate of cartilage that becomes ossified by early adulthood (Mancall and Brock 2011).

The lesser wings of the sphenoid attach to the body anterior to the greater wings. Their superior surface supports the frontal lobe of the brain, while the inferior surface contributes to the posterior portion of the orbital roof and the superior orbital fissure. The levator palpebrae originates from the lesser wing of the sphenoid above the annulus of Zinn.

The greater wings of the sphenoid connect to either side of the lateral surface of the body. The carotid groove is at the anterior extent of this connection and lodges the internal carotid artery and the cavernous sinus. The superior surface of the greater wings contributes to the middle cranial fossa and contains the foramen rotundum and foramen ovale for the transmission of the maxillary (V2) and mandibular (V3) divisions of the

trigeminal nerve, respectively. The foramen spinosum at the posterolateral tip of the greater wing transmits the middle meningeal vessels and a recurrent branch of the mandibular nerve.

Along the inferior surface of sphenoid bone's greater wing is the orbital surface that forms the posterior aspect of the orbit's lateral wall, contributing the posterolateral boundary of the inferior orbital fissure, while its medial margin forms the lower boundary of the superior orbital fissure. Beneath the superior orbital fissure is a grooved surface forming the posterior wall of the pterygopalatine fossa. The pterygoid processes project from the posterior end of the greater wings.

Function

The sphenoid bone contributes to the base and sides of the skull as well as the floor and walls of the orbits. It is the site of attachment for most muscles of mastication. In addition, it contains fissures and foramen that are traversed by nerves and blood vessels supplying the head and neck.

Clinical Relevance

The optic canal, which is situated within the lesser wing of the sphenoid, serves to carry the optic nerve, ophthalmic artery, and sympathetic fibers into the orbital cavity. The optic nerve dura is continuous with the intracanalicular orbital periosteum, making it susceptible to transmitted force from blunt head trauma that can lead to traumatic optic neuropathy. The injury may be caused by shearing action or by swelling of the optic nerve within the optic canal that disrupts blood supply to the nerve. Orbital hemorrhage and optic nerve sheath hematomas can also precipitate traumatic optic neuropathy by direct compression (Levin et al. 2004).

The sella turcica houses a protrusion off the hypothalamus known as the pituitary gland. The optic chiasm lies on top of the pituitary gland and envelopes the pituitary stalk. Since the sella turcica forms a boney caudal border for the pituitary gland, pituitary tumors often extend upward into the suprasellar region where it can compress the optic chiasm leading to a bitemporal hemianopia, which is pathognomonic for a pituitary tumor in the absence of trauma. Empty sella syndrome is the condition of an underdeveloped pituitary gland.

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Spheric Intraocular Lens

▶ Spherical Intraocular Lens

Spherical Equivalent

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Synonyms

Best spherical lens

Definition

Spherical equivalent is the characteristic value of a spherocylindrical spectacle or contact lens which shows the astigmatic eyes ametropia, whether it's myopic or hyperopic. Spherical equivalent can be calculated from the prescription given by the spectacle lens. It is the arithmetic numeric value between the two principal meridians of an astigmatic lens.

Cross-References

- ▶ Ametropia: Definition
- ▶ Diopter: Definition

Spherical Intraocular Lens

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Synonyms

Spheric intraocular lens; Spherical IOL

Definition

Spherical means having the morphological form of a sphere, globular. A spherical intraocular lens is an IOL that has a spherical shape (Auffahrt 2008).

Epidemiology

The number of implanted spherical IOLs is constantly decreasing since aspheric IOL designs are increasing and their superior optical quality especially in contrast sensitivity under mesopic conditions compared to spherical IOLs has been proven in various studies.

History

Since it has been known that the cornea with its prolate surface has a lower refractive index in its periphery in the 1970s and that the human cornea has a positive asphericity, aspheric lenses started to be developed with no or negative spherical aberration. In 2002 the Tecnis IOL (Advanced Medical Optics, AMO) was the first aspheric lens to receive Food and Drug Administration (FDA) approval in the USA. Since the advent of the original Tecnis IOL, two other aspheric monofocal lenses have joined the mix and received FDA clearance: the LI60 AO (Bausch and Lomb), which corrects a smaller amount of spherical aberration than the Tecnis, and the AcrySof IQ IOL (Alcon), which is designed to reduce spherical aberration that is induced by the IOL.

Clinical Features

Upon the optical aberrations of the eye, spherical aberration is the most important (el-Hage and Berny 1973). Regarding IOL design four different types of IOL must be differentiated:

- Spherical IOLs that induce spherical aberration (traditional IOLs)
- IOLs inducing no spherical aberration (aspherical neutral)
- IOLs with negative spherical aberration (aspherical correcting)
- IOLs reducing spherical aberration of the eye in a customized fashion (aspherical optimized)

Tests

Any spherical IOL contributes to the positive spherical aberration of the pseudophakic eye. The amount of spherical aberration induced by the IOL can be determined by subtracting the aberration of the corneal surface from that of the entire eye (Kohnen and Koch 2009).

Differential Diagnosis

Aspherical IOL design is provided with monofocal IOLs, multifocal IOLs, accommodative IOLs, toric IOLs, and blue-light filter IOLs today.

Etiology

The term spherical refers to the Latin word "sphericus" meaning round, globular, or orbicular.

Treatment

Aspherical IOLs are implanted like spherical IOLs into the eye. See also entries "▶ Cataract Surgery" and "▶ Intraocular Lens."

Cross-References

▶ Aspherical Intraocular Lens
▶ Cataract Surgery
▶ Intraocular Lens

References

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Spherical IOL

▶ Spherical Intraocular Lens

Spherocylindrical Lenses

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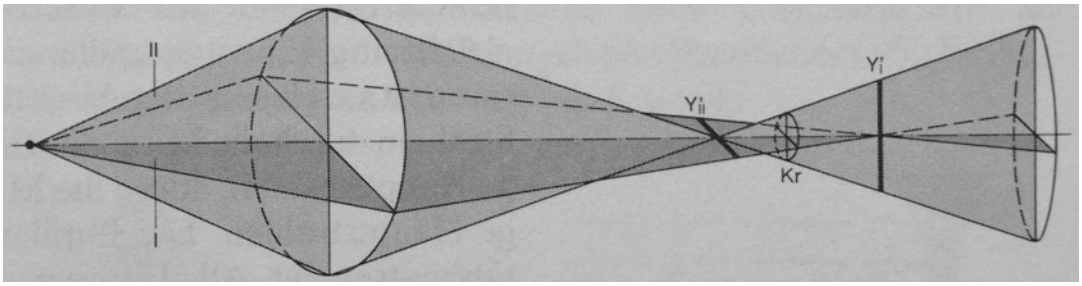
Synonyms

Astigmatic lens; Spherotoric lens; Spherotoroidal lens

Definition

Lenses with spherocylindrical power image a real object point not as an image point, but as two image lines with different image distances. The image lines of an axial object point are perpendicular to the optical axis and lie in the principal meridians lying perpendicularly to each other. The ray bundle of an object point which has a circular cross section at any point prior to refraction exhibits an elliptical cross section subsequent to refraction. The size and shape of the ellipse vary depending on its position. The two image lines are the extremes of the cross section. Between them lies the only point where the cross section of the bundle is circular (instead of a point). The cross section formation (Sturm's conoid) shows this circle of least confusion.

The principal meridian with the mathematically smaller (i.e., weaker positive or stronger negative) refractive power F_β is called the first



Spherocylindrical Lenses, Fig. 1 Sturm's conoid, to demonstrate the nature of astigmatic imagery

S

principal meridian β, while the other is known as the second principal meridian α and has the mathematically larger refractive power F_{α}.

Application: For the correction of astigmatic ametropia.

Cross-References

- ▶ Ametropia: Definition
- ▶ Astigmatism
- ▶ Bitoric

Further Reading

Goersch H (2000) Handbuch für Augenoptik. Carl-Zeiss, D-Oberkochen

Spheroid Degeneration

- ▶ Keratinoid (Spheroidal) Degeneration
- ▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
- ▶ Spheroidal Degeneration

Spheroidal Degeneration

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Synonyms

Several previously reported clinical entities describe globular deposits of the cornea that may represent the same condition, with geographic variations or subtypes:

Band-shaped nodular dystrophy of the cornea; Bietti corneal degeneration; Chronic actinic keratopathy; Climatic droplet keratopathy; Colloid degeneration of the cornea; Degeneratio hyaloidea grannuliformis corneae; Elastoid degeneration; Elastotic degeneration; Eskimo corneal degeneration; Fisherman's keratopathy; Hyaline corneal degeneration; Keratinoid corneal degeneration; Keratoid corneal degeneration; Labrador keratopathy; Nodular corneal dystrophy in tropical arid countries; Proteinaceous corneal degeneration; Sphaerularis elaiodes; Spheroid degeneration; Spheroidal keratopathy; Superficial central primary degeneration oleogutta; The blindness of Dahalach

Definition

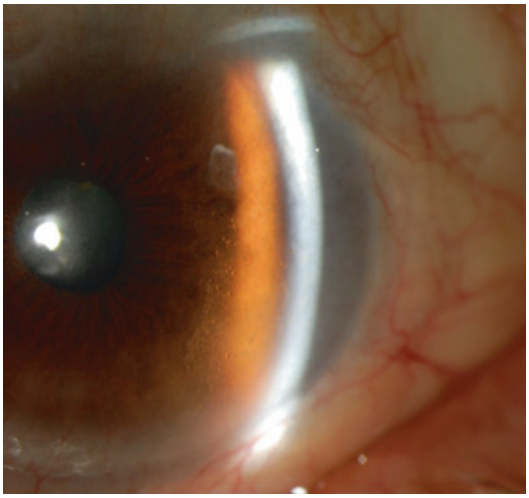
A degeneration of the cornea and/or conjunctiva characterized by the appearance of golden yellow spherules or globules of varying size at or beneath the epithelium.

Etiology

The exact source of the protein material forming the spherules is unknown. It has been postulated that the material may result from the actions of ultraviolet light on serum proteins that diffuse into the cornea from limbal vessels (Farjo and Sugar 2009). Increasing age and exposure to ultraviolet light are the most common associated factors. Other proposed risk factors include dry eyes, malnutrition, corneal trauma or microtrauma (wind, sand, ice), low humidity, and extremes of temperature. Associated ocular diseases include keratitis, lattice corneal dystrophy, and glaucoma (Fraunfelder and Hanna 1973).

Clinical Presentation

Spheroidal degeneration is characterized by the presence of yellow or golden spherules at or beneath the corneal or conjunctival epithelium (Fig. 1). The spherules, or globules, are generally clear but may become more opaque over time and range in size from approximately 0.1 to 0.6 mm in diameter. These lesions are located in the superficial corneal stroma, bowman membrane, subepithelium, and occasionally in the epithelium in advanced degeneration (Magovern et al. 2004).



Spheroidal Degeneration, Fig. 1 Numerous golden spherules are seen in the mid-peripheral, superficial cornea within the palpebral fissure

The clinical presentation has been described as either a primary corneal type associated with age, a secondary corneal type associated with other ocular pathology, and a conjunctival form that may or may not be associated with either type of corneal degeneration (Fraunfelder and Hanna 1973). In the primary form, the lesions are typically seen at the horizontal limbus within the palpebral fissure, and with progression, the spherules enlarge and spread toward the central cornea. In the secondary corneal form, the lesions are less likely to assume a band-shaped configuration and may be concentrated around areas of prior scarring, neovascularization, or inflammation. The lesions are generally bilateral except in secondary cases where there is associated unilateral pathology such as scars, trauma, or keratitis. In the conjunctival form, lesions occur interpalpebrally at the 3 and 9 o'clock positions and are frequently found in association with pinguecula.

Diagnosis

Diagnosis is made clinically based on the characteristic appearance. Biopsy with histologic examination can support or confirm the diagnosis but is not typically required. Histologically, deposits appear as extracellular amorphous globules, which may coalesce to form larger masses in Bowman's membrane (Farjo and Sugar 2009).

Differential Diagnosis

Similar appearing clinical entities include corneal amyloid degeneration, gelatinous drop-like corneal dystrophy (familial subepithelial amyloidosis), band keratopathy, climatic proteoglycan stromal keratopathy, primary lipoidal degeneration of the cornea, Salzmann nodular degeneration, and limbal girdle of Vogt (type II).

Prophylaxis

Unknown. Based on the recognized association with sunlight exposure, it is plausible that methods to reduce sunlight exposure could potentially reduce the development or progression of spheroidal degeneration.

Therapy

Treatment is rarely required since the majority of individuals are asymptomatic. In patients with loss of vision from central corneal lesions, treatment can be considered. Possible treatment options include superficial keratectomy, phototherapeutic keratectomy, lamellar keratoplasty, or penetrating keratoplasty depending on the depth and density of the lesions.

Prognosis

The majority of individuals do not develop any symptoms and progression is slow in the primary form. However, progression may result in loss of vision, particularly in areas of the world where climatic exposure is severe. Visual acuity may be affected due to involvement of the visual axis of the cornea or from irregular astigmatism. In advanced disease, accumulation of globular masses or plaques may cause heaping up of the

corneal surface, epithelial defects, and recurrent corneal erosions. Corneal sensation may be reduced, and sterile ulceration may rapidly progress to microbial keratitis or perforation.

Epidemiology

The prevalence varies based on geographic location with rates of 6% in England and over 60% in males in Labrador (Farjo and Sugar 2009). It is approximately three times more common in males and increases with age, being found in roughly 50% of patients over 70 years of age (Fraunfelder and Hanna 1973). It is most frequently seen in areas with high sunlight exposure. While the primary form is generally considered a degeneration, there are rare reported cases describing a more dystrophic form that may be familial and occur in relatively young patients without a history of other ocular disease or environmental exposure (Santo et al. 1993).

Cross-References

- ▶ Climatic Droplet Keratopathy (Spheroidal Degeneration)
- ▶ Keratinoid (Spheroidal) Degeneration
- ▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)

References

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Magovern M, Wright JD, Mohammed A (2004) Spheroidal degeneration of the cornea: a clinicopathologic case report. Cornea 23:84–88

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Spheroidal Keratopathy

- ▶ Keratinoid (Spheroidal) Degeneration
- ▶ Keratopathy Actinic (Labrador Keratopathy/Spheroidal Degeneration)
- ▶ Spheroidal Degeneration

Spherophakia-Brachymorphia Syndrome

- ▶ Weill-Marchesani Syndrome

Spherotoric Lens

- ▶ Spherocylindrical Lenses

Spherotoroidal Lens

- ▶ Spherocylindrical Lenses

Spinous Keratinocytes

- ▶ Keratinocytes: Overview

Spiradenoma

- ▶ Spiradenoma, Eccrine

Spiradenoma, Eccrine

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Synonyms

Eccrine spiradenoma; Spiradenoma

Definition

A rare, benign tumor of eccrine sweat gland origin.

Etiology

Histopathologically, the tumor involves basophilic cells arranged in rosettes with differentiation towards eccrine secretory cells. A tumor suppressor gene has been suggested in the development of eccrine spiradenomas (American Academy of Ophthalmology 2006–2007; Albert and Jakobiec 2008).

Clinical Presentation

Typically, as 1 cm solitary nodules on the head and neck that are covered by intact skin. Lesions may be intermittently painful. They commonly arise between the ages of 15 and 35 years. Multiple eccrine spiradenomas have been reported in zosteriform and linear patterns. Malignant transformations have been reported in long standing cases and are typically large ulcerated lesions of the trunk and extremities (Beekley et al. 1999; American Academy of Ophthalmology 2006–2007; Albert and Jakobiec 2008).

Diagnostics

Excisional biopsy is necessary to provide definitive diagnosis.

Differential Diagnosis

Adenoid cystic carcinoma
Dermatofibroma
Leiomyoma
Neurolemoma
Poroma

Prophylaxis

Lesions tend not to recur after surgical excision.

Therapy

Surgical excision provides definitive diagnosis. Solitary eccrine spiradenomas are typically benign. Multiple large eccrine spiradenomas may be treated with carbon dioxide laser. Malignant eccrine spiradenoma requires metastatic work-up and consultation with oncologists and radiation oncologists (American Academy of Ophthalmology 2006–2007; Albert and Jakobiec 2008).

Prognosis

Most eccrine spiradenomas are benign and prognosis is excellent. Malignant spiradenomas have been reported to metastasize in 50% of cases and can be fatal (Beekley et al. 1999).

Epidemiology

Eccrine spiradenomas are the rarest of the eyelid adnexal lesions (Fig. 1).

Spiradenoma, Eccrine, Fig. 1 Cystic lesion at the lateral canthus

Cross-References

- ▶ Adenoid Cystic Carcinoma
- ▶ Eccrine Acrospiroma

References

Albert D, Jakobiec F (2008) Principles and practice of ophthalmology, 3rd edn. Saunders, Philadelphia, p 3352

American Academy of Ophthalmology (2006–2007) Basic and clinical science course. Orbit, eyelids, and lacrimal system. 7. p 167

Beekley AC, Brown TA, Porter C (1999) Malignant eccrinespiradenoma: a previously unreported presentation and review of the literature. Am Surg 65(3):236–240

Spiral Computed Tomography, in Orbital Evaluation

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Synonyms

Helical computed tomography

Definition

An imaging technique used to distinguish different tissues by measurement of their different densities using their absorption values after exposure to X-rays.

Purpose

Spiral computed tomography is a useful imaging modality in evaluating patients with orbital disease.

Principle

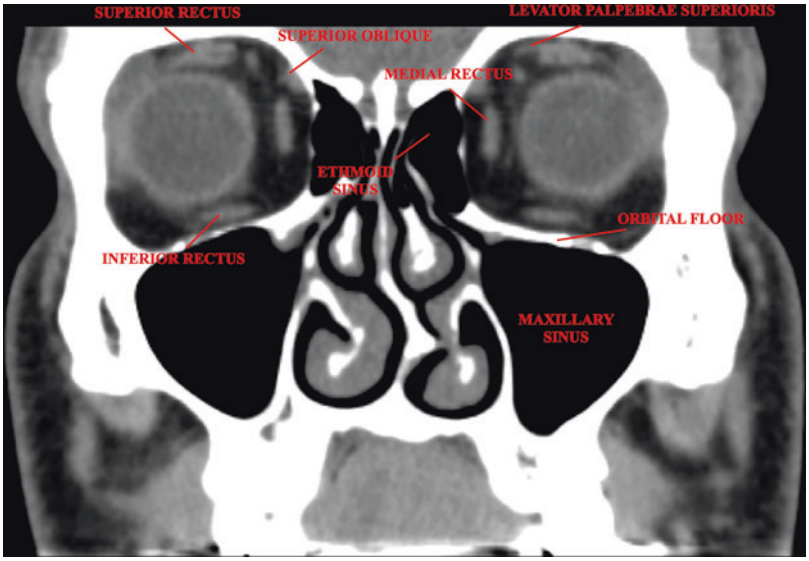
Computed tomography works by using X-ray radiation beams. In comparison to earlier CT units, a spiral CT has multiple detector ports with the scanner and collecting tube moving in a spiral fashion around the patient. This generates a continuous data set that allows for highly detailed reconstructions in all imaging planes. Resolution and tissue-contrast capabilities allow the imaging of soft tissues, bones, foreign bodies, and contrast containing blood vessels (Figs. 1 and 2). This is accomplished using the different absorption values of tissues after the exposure to the X-ray. The final image depends on the tissue attenuation of X-ray, which is denoted by Hounsfield units.

Indication

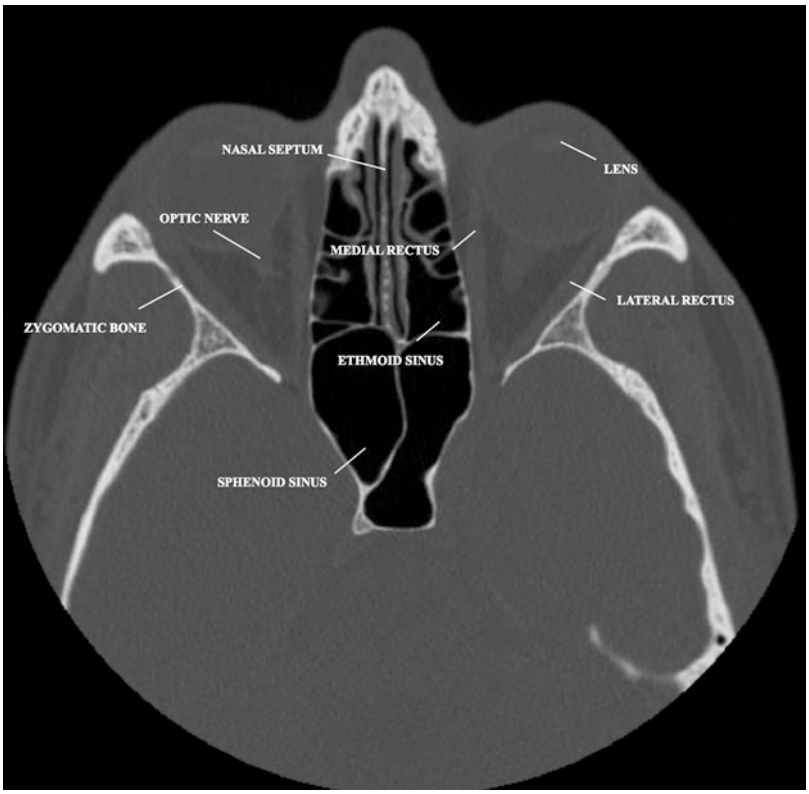
Orbital trauma
Orbital infection
Orbital tumors
Thyroid eye disease
Inflammatory lesions
Proptosis or globe malposition
Preoperative planning

Contraindication

The use of iodine or contrast dye is contraindicated in patients with iodine or contrast allergies and/or renal impairment.



Spiral Computed Tomography, in Orbital Evaluation, Fig. 1 Coronal spiral CT imaging demonstrating orbital and sinonasal anatomy



Spiral Computed Tomography, in Orbital Evaluation, Fig. 2 Axial spiral CT imaging demonstrating orbital and sinonasal anatomy

Advantage/Disadvantage

A spiral CT is a more effective technique for evaluating orbital fractures than traditional plain film X-rays. The short duration of the procedure makes it the preferred technique for orbital evaluation in an emergent situation. The shorter scanning time allows for less motion artifact and patient tolerance. Furthermore, it is safe to use in patients who are

being evaluated for potential metallic foreign bodies.

Disadvantages include exposure to radiation and beam hardening artifacts from metallic objects, including dental fillings. Orbital CTs are also limited in evaluating orbital soft tissue and provides poor definition of the orbital apex in comparison to an MRI.

Cross-References

- ▶ Diffusion-Weighted Magnetic Resonance Imaging
- ▶ Helical Computed Tomography
- ▶ Orbital Cellulitis

References

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Tawfik HA, Abdelhalim A, Elkafrawy MH (2012) Computed tomography of the orbit – a review and update. Saudi J Ophthalmol 26:409–418

Split Foot Syndrome with Clefting

▶ Ectrodactyly-Ectodermal Dysplasial-Clefting (EEC) Syndrome

Split Hand

▶ Ectrodactyly-Ectodermal Dysplasial-Clefting (EEC) Syndrome

Spring Catarrh

▶ Vernal Conjunctivitis/Keratoconjunctivitis

Springing Pupil

▶ Benign Episodic Pupillary Mydriasis

Squamous Carcinoma In Situ

▶ Bowen's Disease

Squamous Cell Cancer (SCC)

▶ Squamous Cell Carcinoma of Eyelid

Squamous Cell Carcinoma of Eyelid

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[2]Department of Ophthalmology, Porto Alegre, Rio Grande do Sul, Brazil

Synonyms

Epidermoid carcinoma; Squamous cell cancer (SCC)

Definition

Malignant skin tumor of squamous (keratinized) epithelium (epithelium that contain squamous cells – thin, flat cells that appear as fish scales microscopically) (Dailey et al. 1994; Albert and Jakobiec 2008; Shields and Shields 2008).

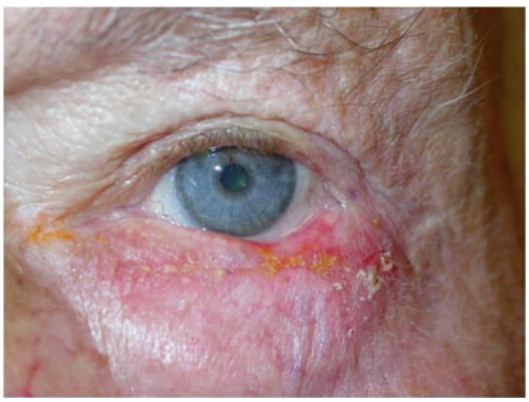
Etiology

SCC arises from the keratin-producing cells of the epidermis (keratinocytes). In the early stages, they

are referred to as squamous cell carcinoma in situ (Bowen's disease). Invasive SCC exhibits extension beyond the basement membrane of the epidermis into the dermis. These tumors can develop spontaneously or in areas of previous actinic keratoses, burns, scars, or chronic ulcers. It is most often encountered in elderly, fair-skinned individuals who have a history of chronic sun exposure. Other risk factors include radiation therapy, exposure to carcinogens, chronic skin irritation or inflammation, genetic diseases (xeroderma pigmetosum, albinism), and presence of premalignant lesions. Squamous cell cancer can also occur after organ transplantation (immunocompromised hosts) (Dailey et al. 1994; Albert and Jakobiec 2008; Shields and Shields 2008).

Clinical Presentation

SCC, although much less common than basal cell carcinoma (BCC), behaves more aggressively. Usually they appear as painless elevations or nodules, often with a pearly appearance, with either loss or distortion of the eyelashes. There may be ulceration of the involved area, with bleeding, crusting, redness, and/or distortion of the normal skin appearance (Fig. 1). Palpation of preauricular and submandibular lymph nodes is important to detect potential metastatic spread (Dailey et al. 1994; Albert and Jakobiec 2008; Shields and Shields 2008).



Squamous Cell Carcinoma of Eyelid, Fig. 1 Squamous cell carcinoma of the left lower eyelid, demonstrating diffuse infiltrative tumor with crusting and ectropion of the eyelid

Diagnostics

Diagnosis is established by biopsy and histopathological confirmation. In some instances, SCCs may be found at the base of a cutaneous horn; therefore it is imperative to examine the base of these types of tumors histologically.

Differential Diagnosis

Differential diagnosis includes basal cell carcinoma, ▶ actinic keratosis, ▶ seborrheic keratosis, ▶ sebaceous carcinoma, ▶ keratoacanthoma, ▶ melanocytic nevus, ▶ melanoma, ▶ trichoepithelioma, and ▶ inverted follicular keratoses.

Prophylaxis

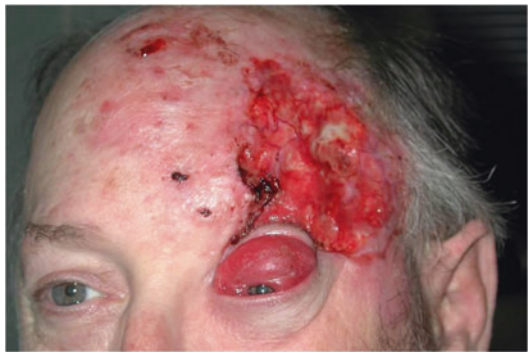
Avoidance of sun exposure; use of sunscreens, sunglasses, and hats.

Therapy

SCC is treated best by early intervention with complete excision (frozen-section control of the margins or with the Moh's technique). Other treatments include radiation, cryotherapy, photodynamic therapy, and systemic chemotherapy but are perhaps not as efficacious as surgical intervention. Extension into the orbit and sinuses may require more extensive surgical intervention (e.g., exenteration, sinusectomy) with subsequent radiation therapy (Dailey et al. 1994; Albert and Jakobiec 2008; Shields and Shields 2008).

Prognosis

The prognosis is excellent if the lesion is detected early and completely excised. Prognostic factors



Squamous Cell Carcinoma of Eyelid, Fig. 2 Extensive SCC with massive diffuse involvement of eyelid and orbit invasion

include the degree of differentiation, the etiology, tumor size, and the immune status of the patient. Unlike BCC, SCC has the ability to invade local tissues (orbital invasion) and metastasize to lymph nodes and distant sites (Fig. 2). Perineural spread is another adverse prognostic sign (Dailey et al. 1994; Albert and Jakobiec 2008; Shields and Shields 2008).

Epidemiology

SCC represents approximately 5–10% of all eyelid malignancies. It is the second most common form of skin cancer after BCC (Dailey et al. 1994; Albert and Jakobiec 2008; Shields and Shields 2008).

Cross-References

- Actinic Keratosis
- Conjunctival Nevus
- Inverted Follicular Keratosis
- Keratoacanthoma
- Melanoma of the Eyelid
- Sebaceous Carcinoma
- Seborrheic Keratosis
- Trichoepithelioma

References

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Squamous Cell Carcinoma, of the Conjunctiva

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Synonyms

Conjunctival squamous cell carcinoma

Definition

An abnormal proliferation of dysplastic cells arising within the epithelial layer of the conjunctiva. Various histopathological abnormalities including but not limited to cellular pleomorphism, increase in mitotic figures, suprabasal mitotic figures, and a decrease in desmosomal/hemidesmosomal attachments can be seen. When the dysplastic cells penetrate the epithelial basement membrane and invade the subepithelial connective tissue, the lesion becomes an invasive squamous cell carcinoma.

Etiology

It is caused by disordered maturation of the epithelium. Ultraviolet B radiation, which can cause point mutation in the p53 tumor suppressor gene, human papillomavirus (types 16 and 18), and

immunosuppression (often due to HIV) have been implicated in the pathogenesis of this disease (Tunc et al. 1999).

Clinical Presentation

Some common presenting symptoms include eye redness, foreign body sensation, pain and tearing. Conjunctival squamous cell carcinoma usually arises in the interpalpebral, perilimbal conjunctiva as a slightly elevated, well-demarcated lesion, accompanied by feeding blood vessels. The lesion can also be nodular, gelatinous, pigmented, or diffuse. It can sometimes mimic benign conjunctival degeneration or chronic conjunctivitis (Hamam et al. 2009).

Diagnosis

It is generally diagnosed by excisional biopsy, although cytologic analysis is sometimes used. Microscopic analysis shows dysplastic changes involving most or all of the epithelial thickness, often with sharp demarcation from normal conjunctiva at the peripheral borders. Extension through the epithelial basement membrane and involvement of the subepithelial tissue distinguish invasive carcinoma from in situ tumors. Immunohistochemical staining can show expression of the oncogene p63 and mutant tumor suppressor gene p53, although these are not specific (Hamam et al. 2009). It is staged according to the tumor-node-metastasis (TNM) staging system developed by the American Joint Committee on Cancer (AJCC) and Union for International Cancer Control (UICC).

Differential Diagnosis

Dermoid, dyskeratosis, conjunctival intraepithelial neoplasia, intraepithelial sebaceous neoplasia, lymphoproliferative process, papilloma, pingueculum, scar tissue, conjunctival melanoma, and chronic conjunctivitis.

Prophylaxis

There are no proven prophylaxes.

Therapy

Therapy consists of surgical excision, usually accompanied by adjuvant cryotherapy and/or adjuvant topical therapy with mitomycin (MMC), 5-fluorouracil (5FU), or interferon alpha 2b. For nonresponsive carcinomas, palliative treatment with subconjunctival ranibizumab and external beam radiation therapy (photons, electrons, or protons) have also been used (Yousef and Finger 2012).

Prognosis

Reported local recurrence rate varies widely and can be as high as 50% (Zaki and Farid 2009) when there is residual tumor in the surgical margins. Risk factors for tumor recurrence include tumor size larger than 5 mm, larger than 2 mm extension onto the cornea, and tumor local invasiveness (Yousef and Finger 2012). Intraocular invasion has been reported to happen in 2–8% (Tunc et al. 1999) of the cases. Metastases are rare. The first sites of metastasis are the preauricular and submandibular regional lymph nodes, but more distant metastases to the parotid gland, lungs, and bone have also been reported (Yousef and Finger 2012). Surgical excision with adjuvant therapy carries a higher rate of cure, compared to surgical excision alone. Surgical excision with adjuvant cryotherapy, topical MMC, topical 5FU, or topical interferon alpha 2b has a cure rate of at least 80% (Hamam et al. 2009).

Epidemiology

The disease affects all racial groups of all ages. However, it has a slight male predominance, with an average age of onset in the 50s. Fair-skinned populations at latitudes closer to the equator may be at a higher risk, and xeroderma pigmentosum is associated with an increased risk of earlier

development of this condition. The average annual incidence of conjunctival squamous cell carcinoma has been estimated to be 17–20 cases per million persons per year (Hamam et al. 2009).

References

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Squamous Cell Papillomas of Eyelid

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[2]Department of Ophthalmology, Porto Alegre, Rio Grande do Sul, Brazil

Synonyms

Acrochordon; Papilloma; Skin tag; Squamous papilloma

Definition

Benign hyperplasia of squamous epithelium of the skin (Albert and Jakobiec 2008; Shields and Shields 2008).

Etiology

Due to UV, other cell damage, but most often arise de novo. Papillomas represent benign overgrowths of normal epithelium, with varying levels of keratinization and pigmentation.

Clinical Presentation

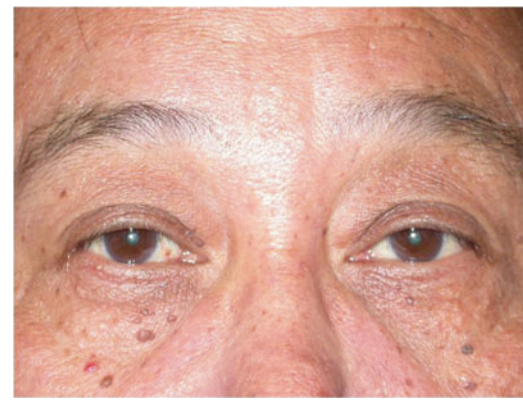
Squamous cell papilloma (SCP) may be pedunculated, sessile, solitary, multiple, pigmented, or same color of the skin. Sessile papilloma often has a broad base and a smooth surface (Fig. 1). Unlike pedunculated papilloma, it has a rough and cerebriform convoluted surface (Fig. 2). The onset is gradual and with slow growth. Much more common in middle age or elderly individuals. In rare instances, they represent precancerous lesions, so malignant conversion remains a consideration (Albert and Jakobiec 2008; Shields and Shields 2008).

Diagnostics

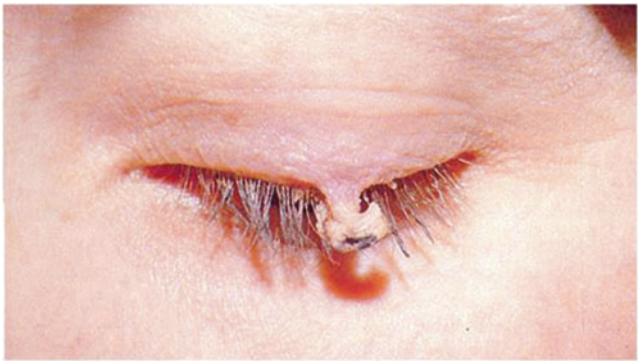
Biopsy and histopathologic interpretation.

Differential Diagnosis

Differential diagnosis includes ▶ melanocytic nevus, ▶ basal cell carcinoma ▶ seborrheic keratosis, ▶ fibroma, ▶ Verruca Vulgaris, and ▶ actinitic keratosis.



Squamous Cell Papillomas of Eyelid, Fig. 1 Woman with squamous papillomas on upper and lower eyelids



Squamous Cell Papillomas of Eyelid, Fig. 2 Pedunculated papilloma arising on upper eyelid

Prophylaxis

Avoidance of sun and UV exposure (use of sunscreens, sunglasses, umbrellas, and hats).

Therapy

Usually serial observation or surgical excision of the lesion. If any signs of malignancy develop, biopsy and removal are essential. Treatment is complete surgical resection. When surgery is not appropriate or possible, radiotherapy, cryotherapy, or pharmacotherapy can be considered.

Prognosis

Excellent with little risk of malignant transformation.

Epidemiology

Common; perhaps the most common eyelid benign lesion.

Cross-References

- ▶ Actinic Keratosis
- ▶ Actinic (Solar) Keratosis
- ▶ Basal Cell Carcinoma of Eyelid
- ▶ Vascular Nevus
- ▶ Verruca Vulgaris

References

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Squamous Cells

- ▶ Keratinocytes: Overview

Squamous Dysplasia of Conjunctiva

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Synonyms

Conjunctival intraepithelial neoplasia (CIN); Conjunctival squamous dysplasia

Definition

Conjunctival intraepithelial neoplasia (CIN), or dysplasia, is analogous to actinic keratosis of the eyelid skin. In CIN, the dysplastic process does not invade the underlying basement membrane and is classified in mild, moderate, or severe,

according to the degree of the extension and amount of atypical cells involving the epithelium.

Etiology

The conjunctiva is a mucus membrane as many others in the body but is different because it is partially exposed to the sun. The relative contributions to this condition such as HPV infection, chronic sunlight exposure, and host factors have not been determined yet. Exposure to tobacco, petroleum products, and history of HIV infection may be predisposing factors for rapidly progressive and aggressive diseases.

Clinical Presentation

Individuals with CIN clinically present with symptoms ranging from foreign body sensation, redness, and irritation to an evident growth on the ocular surface that may be a potential cause of visual loss.

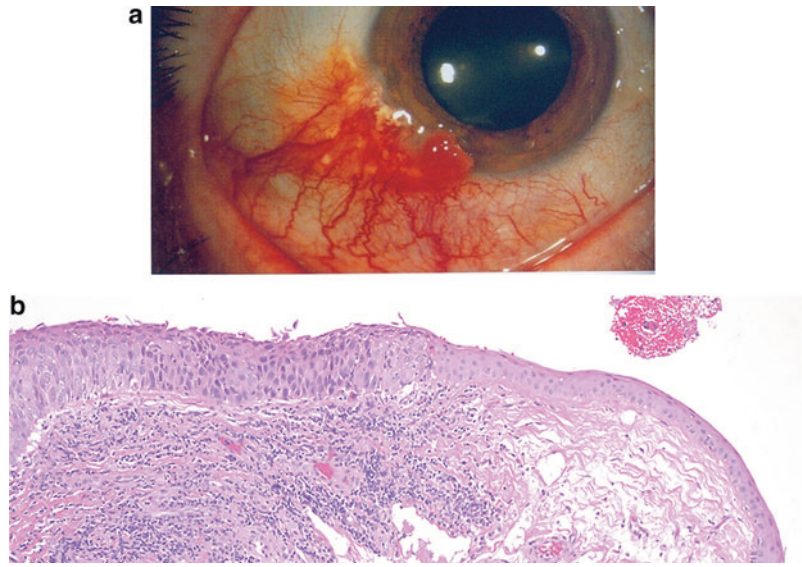
CIN is usually found at the limbus in the interpalpebral zone (Fig. 1a). There are three principal clinical variants:

1. Papilliform, in which a sessile papilloma harbors dysplastic cells
2. Gelatinous, as a result of acanthosis and dysplasia
3. Leukoplakic, caused by hyperkeratosis, parakeratosis, and dyskeratosis

Mild inflammation and various degrees of abnormal vascularization may accompany CIN lesions, but large feeder blood vessels indicate a higher probability of invasion beneath the epithelial basement membrane. CIN lesions are slow-growing tumors, nearly always centered at the limbus but with the potential to spread to other areas of the ocular surface, including the cornea.

Diagnosis

Histologically, CIN typically shows an abrupt transition between normal conjunctival epithelium and the dysplastic epithelium, which are characterized by hyperplasia, loss of normal cell polarity, nuclear hyperchromasia, pleomorphism, mitotic figures, and in some cases, goblet cell loss (Fig. 1b). There is often surface keratinization, correlating with the leukoplakia observed clinically. Dyskeratosis (non-surface cells producing keratin) may also be seen. A chronic inflammatory response is often present in the substantia propria.



Squamous Dysplasia of Conjunctiva, Fig. 1 (**a**) Clinical presentation. (**b**) Histopathology finding

It is important to perform an adequate histological evaluation in order to classify the degree of epithelial dysplasia, and whether or not, the lesion is contained by the basement membrane. The epithelial dysplasia may be graded as mild, moderate, or severe, according to the degree of cellular atypia.

Differential Diagnosis

- Squamous cell carcinoma
- Limbal stem cell deficiency
- Squamous papilloma
- Pterygium
- Pinguecula

Therapy

Surgical excision of OSSN with or without cryotherapy or brachytherapy is still commonly performed; however, in the last decade, topical chemotherapy using mitomycin C, 5-FU, and interferon alfa-2b has become popular in the treatment of CIN.

Prognosis

Although the histopathologic grading and evaluation play an important role, distinguishing in between the extent of disease does not necessarily have clinical utility in terms of prognosis.

In cases with the most severe atypia, full-thickness involvement of the epithelium is seen, often with squamous eddies or keratin whorls/pearls. For these more advanced lesions, the term squamous carcinoma in situ may be used. If, however, the neoplastic cells have invaded the stroma, then the diagnosis is invasive squamous cell carcinoma. Clinically, the term CIN has fallen out of favor in preference to the more general term OSSN, because it is not possible to determine on clinical examination whether stromal invasion has occurred. CIN should be regarded as a histologic term, reserved for noninvasive lesions. Invasion through the sclera or cornea and intraocular spread are uncommon complications of invasive squamous carcinoma.

Epidemiology

CIN affects men more than women; it is associated to chronic sun exposure and tobacco.

References

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Squamous Papilloma

► Papillomas, Eyelid
► Squamous Cell Papillomas of Eyelid

Standing Potential of the Eye

► Electrooculogram

Staphylococcal Hypersensitivity Keratitis

► Catarrhal (Marginal Corneal) Infiltrates

Staphylococcal Marginal Disease

▶ Catarrhal (Marginal Corneal) Infiltrates

Staphylococcus

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Synonyms

Staphylococcus aureus

Definition

Staphylococcus aureus is the most common infectious agent that causes chronic blepharitis. Other ocular complications include acute and chronic bacterial conjunctivitis (with mucopurulent discharge), phlyctenular conjunctivitis, corneal inflammation, dacryoadenitis, and hordeolum. Methicillin-resistant *Staphylococcus aureus* (MRSA) can cause bilateral blindness from orbital cellulitis, panophthalmitis, and complete corneal flap melt after LASIK.

Cross-References

▶ Blepharitis
▶ Conjunctivitis
▶ Dacryoadenitis
▶ External Hordeolum (Stye)
▶ Hordeolum
▶ Laser in Situ Keratomileusis
▶ Orbital Cellulitis
▶ Phlyctenules

Staphylococcus aureus

▶ *Staphylococcus*

Staphylomas, Congenital, Anterior

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Synonyms

Congenital corneal ectasia; Keratectasia

Definition

Congenital anterior staphyloma refers to severe thinning and bulging of the cornea or sclera which is present at birth.

Etiology

Although no single theory exists on its etiology, congenital anterior staphyloma is generally thought to occur as a result of abnormal embryologic migration of mesenchymal tissues. Other theories proposed include in utero exposure of infectious or inflammatory conditions resulting in corneal thinning (Sugar and Wadia 2009).

Clinical Presentation

The infant typically presents at birth with corneal opacity and bulging of the anterior segment through the palpebral fissure beyond the eyelid plane, resulting in a "flask-shaped" eye. Exposure keratopathy can occur, which can lead to epithelial metaplasia and keratinization. The anterior sclera may be very thin and transparent but is typically of normal thickness starting posterior to the rectus muscle insertion (Watson et al. 2012). Because of the disorganization of anterior segment structures, glaucoma is a common sequela of this disease from anterior synechiae leading to secondary angle closure. This condition may be unilateral or bilateral (Leff et al. 1986).

Acquired anterior staphylomas may occur in the setting of scleral inflammation with constant and prolonged increased intraocular pressure >40 mmHg, such as in chronic anterior uveitis or rheumatoid scleritis combined with secondary glaucoma. This results in the protrusion of uvea through an inflammatory scleral defect. Acquired anterior scleral staphylomas may also occur in the setting of trauma, surgery, or overlying masses (Watson et al. 2012).

Diagnostics (Lab Diagnostics)

Laboratory markers are not utilized in the diagnosis of congenital anterior staphylomas, but histopathological studies have helped to identify this condition. Corneal specimens have shown an irregular epithelium, attenuated Bowman's layer, stromal thickening with vascularity, and absent Descemet's membrane and endothelium corresponding with the area of posterior uveal lining (Zein and Mokhtarzadeh 2013). A detailed fundus exam should also be performed to assess the viability of posterior segment structures.

Differential Diagnosis

The differential diagnosis for congenital anterior staphylomas includes Peters anomaly, anterior segment dysgenesis, keratoglobus, buphthalmos, pigmented conjunctival tumor, extraocular extension of a ciliary body melanoma, or foreign body (Shields et al. 2003; Watson et al. 2012).

Prophylaxis

No known prophylactic measures to prevent congenital anterior staphylomas have been noted to date.

Therapy

Congenital anterior staphylomas may be managed with penetrating keratoplasty, not only for visual rehabilitation but also for cosmetic appearance. The success of penetrating keratoplasty is not well studied in these patients and is highly variable based on disease severity.

Prognosis

Visual prognosis is poor for infants born with this condition. Enucleation is often necessary if the eye becomes blind and painful.

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Stargardt Disease

▶ Fundus Flavimaculatus (Stargardt Disease/Juvenile Macular Degeneration)

Stargardt Macular Dystrophy

▶ Fundus Flavimaculatus (Stargardt Disease/Juvenile Macular Degeneration)

Steatoblepharon

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Definition

The word steatoblepharon comes from steato, which means fat, and blepharon, which means eyelid. It refers to the herniation of orbital fat from the eyelids. "Eyelid bags" is a more general term used to encompass all the factors, including steatoblepharon, that cause outpouching of the eyelids.

Etiology

Orbital fat is contained by the orbital septum and protrudes causing steatoblepharon. It has been observed that steatoblepharon occurs from aging with several studies describing volume loss and gravitational effects on the orbital septum as contributing factors. Over time, the orbital septum may become more lax, and fat can prolapse forward resulting in steatoblepharon. Volume loss of the overlying skin may also contribute to the prominence of the fat.

Clinical Presentation

Steatoblepharon presents as outpouching of the overlying eyelid skin with fullness of the eyelids. It is often found along with ptosis, dermatochalasis, and other effects of aging.

Diagnostics

Diagnosis is made clinically by observation.

Differential Diagnosis

Steatoblepharon from aging should be differentiated from other causes of masses or edema around the eyes including malignancy, thyroid eye disease, or trauma. Other factors that can cause eyelid bags include eyelid fluid and loss of the elasticity of the skin.

Therapy

The treatment for steatoblepharon is surgery, usually as a part of blepharoplasty to remove the excess protruding skin and prolapsed fat. During blepharoplasty the orbital septum and periorbital fat can be shaped or removed by cautery to improve the steatoblepharon.

Further Reading

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Lambros V (2007) Observations on periorbital and midface aging. Plast Reconstr Surg 120(5):1367–1376
Mally P et al (2014) The role of gravity in periorbital and midfacial aging. Aesthet Surg J 34(6):809–822

Steele-Richardson-Olszewski Syndrome

► Progressive Supranuclear Palsy

Steep Central Islands

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Synonyms

Central island

Basic Characteristics

Result of an incomplete excimer laser ablation with a broad beam laser. Plumes of the ablation gathered over the central cornea lead to an incomplete ablation at the corneal center. Topography shows a marked central area of increased curvature, often with local irregularities. Central steep islands are associated with reduced visual acuity (Krueger et al. 1996).

Other corneal conditions that result in a central corneal steepening such as central keratoconus, local iatrogenic keratectasia, corneal laser refractive surgery for hyperopia or presbyopia, and central scars may mimic a central steep island. Particularly, the creation of a hyperprolate cornea with presbyopia excimer treatments results in a central steep island.

The treatment of central steep islands is difficult. A rigid gas-permeable contact lens may improve image quality by correcting corneal higher-order aberrations. The surgical treatment with topography-guided laser refractive surgery turned out to be difficult and rarely satisfying.

Cross-References

► Photorefractive Keratectomy (PRK)

References

Krueger RR, Saedy NF, McDonnell PJ (1996) Clinical analysis of steep central islands after excimer laser photorefractive keratectomy. Arch Ophthalmol 114:377–381

Stem Cells, Limbal, Corneal Epithelium Maintenance

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Definition

Adult corneal stem cells are undifferentiated progenitor cells capable of rapid proliferation and self-renewal. Stem cells are capable of producing large numbers of differentiated progeny, which help maintain the corneal surface epithelium. They play an important role in wound healing through continued replacement and regeneration of the tissue.

Structure

There are several features that help to distinguish between the limbus and the central cornea. The limbal epithelial stem cells display a slower turnover cycle and consist of a thicker cell layer (eight to ten cells) than the corneal epithelium (five cells). The heavier pigment in the limbus may help protect these cells from sun damage that could lead to the development of malignant lesions. The limbal stroma's vascularity and innervation provide the ideal environment for stem cell growth and proliferation. Limbal blood vessels provide nutrients to the limbal epithelium and may contribute to the higher concentrations of Na^+/K^+ ATPase and carbonic anhydrase in the basal cells of the limbal epithelium. It is not clear yet whether these proteins are involved in cellular regulatory functions. Within the palisades of Vogt, the epithelial and stromal cells have a stronger physical connection making the stem cells less susceptible to trauma. The most common cause of limbal stem cell deficiency is destruction of those cells by chemical, thermal, or cryo-injuries, Stevens-Johnson syndrome, pemphigoid, radiation, and surgical trauma. Another less common cause is aniridia

Function

Under normal circumstances stem cells remain dormant and do not replicate frequently. This dormant state minimizes errors during cell division. In the presence of an epithelial injury, unique environmental and cellular characteristics allow stem cells to respond quickly. To do so stem cells give rise to amplifying cells. These amplifying cells have a shorter replication cycle and increased cell division. This translates into increased efficiency by increasing stem cell

division without increasing proliferation. Limbal basal cells express higher concentrations of epidermal growth factor receptor, $Na^{-}K^{-}$ATPase, cytochrome oxidase, and carbonic anhydrase. They also express intermediate fibers accounting for the stronger cellular adhesions in that area.

Clinical Relevance

The main function of the corneal epithelium is to provide a barrier against pathogens and to minimize trauma to the underlying stroma. Limbal stem cells help maintain an intact corneal epithelium by dispatching new basal cells into the central cornea. In the presence of an epithelial defect, surgically induced or as a result of other trauma, limbal basal stem cells rapidly proliferate to repopulate the surface defect.

Patients with stem cell deficiency may present with pain, decreased visual acuity, photophobia, redness, or tearing. In a cornea with limbal stem cell deficiency, an irregular dull corneal reflex can be demonstrated by slit lamp biomicroscopy. It may also present with chronic or recurrent epithelial defects. Limbal stem cell deficiency can ultimately lead to corneal scarring, vascularization, or perforation. Mildly symptomatic patients can be treated with artificial tears or lubricating ophthalmic ointments. Those with partial stem cell deficiency that present with visual impairment or chronic epithelial defects may benefit from surgical interventions such as epithelial debridement with close follow-up to monitor surface healing. Debridement can also be combined with amniotic membrane transplantation. Extensive stem cell deficiency may require limbal stem cell transplantation. The tissue used in this procedure can be an autograft from the fellow eye or allograft from a living relative or cadaver donor. Stem cell transplantation can be combined with amniotic membrane transplantation in patients with chemical burns, Stevens-Johnson syndrome, or cicatricial pemphigoid.

Patients receiving a limbal allograft are at high risk of an immunologic reaction to the transplanted cells. Immunosuppression can be achieved with cyclosporine-A or FK-506. The duration of treatment may be indefinite. The risk of rejection may be reduced by using HLA-matched cells.

Cross-References

- ▶ Basal Cell Epithelioma
- ▶ Corneal Epithelial Cysts

Further Reading

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Steroid Hormone

- ▶ Corticosteroids

Steroids

- ▶ Corticosteroids, Use in Ophthalmology

Stevens Johnson Syndrome

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Synonyms

Erythema multiforme major

Definition

Stevens-Johnson syndrome (SJS) is a severe autoimmune disease of the skin and mucous membranes with potentially devastating ocular consequences, and is part of a spectrum of similar disorders including erythema multiforme, and toxic epidermal necrolysis (TEN).

The term *Erythema multiforme major* is used interchangeably with SJS; erythema multiforme minor primarily involves the skin and at most one mucosal surface. In contrast, SJS by definition involves skin lesions and two or more mucosal surfaces, along with other systemic and ocular manifestations (Friedman and Kaiser 2007; Krachmer et al. 2011; Hoyt and Taylor 2012).

Etiology

SJS is commonly triggered by a drug reaction (i.e., sulfonamides, penicillin, salicylate, barbiturates, isoniazid, or phenytoin) or infection (HSV, adenovirus, *Mycoplasma*, and *Streptococcus* species). Drug toxicity is responsible for 50–60% of SJS cases. Sulfonamides are the most common drugs associated with SJS in healthy patients and those with HIV. Frequently used ophthalmic drops such as scopolamine, sulfonamide, dorzolamide, or tropicamide have all been associated with SJS.

SJS is considered to be a cell-mediated immune response to certain drugs and infectious agents, although exact mechanisms of disease have yet to be fully elucidated. The cause of skin and mucosal lesions involves Fas-Fas ligand interaction and cytotoxic T-lymphocyte activation resulting in keratinocyte apoptosis. Certain HLA markers have been associated with SJS; patients with the ocular lesions of SJS have a significantly raised incidence of HLA-B12, HLA-B44, HLA-Aw33, and HLA-DRw53.

In the eye, SJS triggers a nonspecific inflammatory response in the acute phase affecting subepithelial layers of conjunctiva. Collagen associated with arterioles and venules undergoes fibrinoid necrosis. In the chronic phase, the most prominent finding is cicatrization of the cornea, conjunctiva, and eyelids. In turn, conjunctival mucus-producing goblet cells decrease in number. A subsequent increase in basal epithelial cells and conjunctival cells correlates with disease severity (Friedman and Kaiser 2007; Krachmer et al. 2011; Hoyt and Taylor 2012).

Clinical Presentation

After 1–3 weeks of initial exposure or hours after re-exposure to the inciting agent, a characteristic systemic prodrome of fever, headache, malaise, arthralgia, and upper respiratory infection precedes dermatologic and ocular features. Days later, skin eruptions and ocular involvement causing decreased vision, pain, redness, and swelling occur. Skin lesions begin as erythematous macules and target lesions which progress to vesicular lesions and necrosis. In severe disease, Nikolsky's sign may be present, in which the outer epidermis undergoes exfoliation with light rubbing. Any mucosal surface can also be affected and show ulceration and strictures; lesions are commonest on the lips and oral mucosa.

Ocular manifestations of SJS and TEN can be severe, involving the bulbar and palpebral conjunctiva, eyelids, and cornea. Acute ocular complications, especially initial nonspecific conjunctivitis, may occur concurrently with the skin disease or precede it by several days. The bilateral conjunctivitis may be catarrhal or pseudomembranous. It may occur in 15–75% of patients with SJS. It is characterized by decreased visual acuity, conjunctival injection, mucous discharge, membranes, symblepharon, and trichiasis. Corneal ulceration, scarring, vascularization, and keratinization may also appear as a result of conjunctival scarring involving the lid margin, tarsus, and loss of the fornix.

The initial eye findings may resolve in 2–4 weeks. Late complications arise due to damage to the limbal epithelial stem cells and chronic inflammation or infection causing corneal opacity and neovascularization. Patients may develop chronic irritation of the cornea as a result of entropion, trichiasis, and lid margin keratinization. This may occur due to lacrimal duct cicatrization with destruction of the conjunctival goblet cells.

The level of corneal scarring is proportional to the severity of eyelid margin and tarsal pathology (Friedman and Kaiser 2007; Krachmer et al. 2011; Hoyt and Taylor 2012).

Diagnosis

A comprehensive history may reveal a causative agent in patients with suspected SJS. The diagnostic criteria for SJS are as follows:

- Less than 20% of body area involved in first 48 h
- Greater than 10% body area involvement
- Target (iris) lesions (typical or atypical)
- Individual lesions less than 3 cm in diameter (lesions may coalesce)
- Mucous membrane involvement (at least two areas)
- Fever
- Biopsy specimen compatible with erythema multiforme major

The eye exam should evaluate the lids for trichiasis, conjunctiva for injection, symblepharon, and ulceration, and the cornea for staining, ulceration, and scarring. During the acute phase of the disease, inspection of the skin and oral mucosa should be conducted which may reveal characteristic lesions (Friedman and Kaiser 2007; Krachmer et al. 2011; Hoyt and Taylor 2012).

Differential Diagnosis

Cicatricial pemphigoid may present with similar findings as chronic ocular manifestations of SJS. Symblepharon presents with more severity in cicatricial pemphigoid. Other disorders in the differential diagnosis include squamous cell carcinoma, scleroderma, sarcoidosis, ocular rosacea, and severe chronic keratoconjunctivitis caused by bacteria, viruses, medications, allergies, chemical burns, avitaminosis A, and trachoma. A useful diagnostic tool is the comprehensive history which may reveal a drug reaction with the typical skin and mucosal lesions of SJS (Friedman and Kaiser 2007; Krachmer et al. 2011; Hoyt and Taylor 2012).

Prophylaxis

Prophylactic use of IVIG in on-going trials has shown benefits in patients with previous SJS episodes. Agents most commonly associated with SJS should be avoided (Friedman and Kaiser 2007; Krachmer et al. 2011; Hoyt and Taylor 2012).

Therapy

During the acute stage of SJS, frequent conjunctival irrigation and prophylactic antibiotics may be used to prevent secondary infection. Corneal and conjunctival epithelium should be lubricated with artificial tear supplements. Cycloplegics may be used for presence of anterior uveitis. Careful use of topical steroids may decrease inflammation but increase risk for secondary infection. Symblepharon may be treated with daily lysis, clear plastic wrap, or a symblepharon ring. The treatment goal of ocular surface stability and termination of inflammatory process may necessitate amniotic membrane application over the conjunctiva and cornea.

Management goals of the chronic stages are to restore eyelid and forniceal anatomy and function, supply tear function, and restore the ocular surface. Artificial tear use may treat keratoconjunctivitis sicca that develops due to scarring of the conjunctiva and lacrimal ducts. Abnormal mucous discharge can be managed by administration of mucolytic agents such as 10% *N*-acetylcysteine. Management of epithelial defects may require use of bandage soft or gas-permeable contact lenses.

Surgical intervention includes tarsorrhaphy which can be used to improve the status of the ocular surface. Keratolimbal allograft may be used in select cases for the treatment of persistent epithelial dysfunction. Penetrating keratoplasty can be performed to improve vision once the epithelium has been stabilized; however, severe

cases unable to support a penetrating keratoplasty graft may benefit from keratoprosthesis. Topical transretinoic acid can also be applied to reverse conjunctival transdifferentiation following ocular surface injury (Friedman and Kaiser 2007; Krachmer et al. 2011; Hoyt and Taylor 2012).

Prognosis

The mortality rate of SJS is approximately 1–5%. The disease is usually self-limiting, but mucous membrane damage is permanent and chronic ocular complications may portend a devastating prognosis. In fact, it is the eye disease in SJS that causes substantial long-term morbidity (Friedman and Kaiser 2007; Krachmer et al. 2011; Hoyt and Taylor 2012).

Epidemiology

The annual incidence in all ages is approximately 1.9 in 1,000,000 individuals, higher among HIV positive patients. Approximately, 80% of patients hospitalized for treatment of SJS develop eye disease and 35% experience chronic ocular changes (Friedman and Kaiser 2007; Krachmer et al. 2011; Hoyt and Taylor 2012).

Cross-References

- ▶ Amniotic Membrane Transplantation Nonpharmacotherapy
- ▶ Keratoconjunctivitis: Overview
- ▶ Keratoconjunctivitis, Sicca: Definition
- ▶ Pemphigoid, Cicatricial
- ▶ Pseudomembrane, Conjunctival
- ▶ Symblepharon
- ▶ Tarsorrhaphy
- ▶ Trichiasis

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Stickler Syndrome (Hereditary Progressive Arthro-Ophthalmopathy)

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Synonyms

Hereditary progressive arthro-ophthalmopathy; Stickler syndrome membranous vitreous type; Stickler syndrome vitreous type I

Definition

Stickler syndrome type I is an autosomal-dominant progressive chondrodysplasia associated with vitreoretinal degeneration. It produces a variety of ocular, orofacial, and skeletal abnormalities.

Etiology

Stickler syndrome (type I) is due to an abnormality in the structural gene for type II collagen (COL2A1) on chromosome 12q13.11-q13.2. Most commonly, the abnormality is a premature stop codon mutation which produces COL2AI haploinsufficiency. Missense mutations can also occur. Stickler syndrome type I is different from Stickler syndrome type II, which involves an abnormality of the COL11A1 gene. Stickler syndrome type I is also different from Stickler syndrome type III, which displays no ocular abnormalities (Carr and Noble 1999; Edwards and Robertson 2006).

Clinical Presentation

Patients with Stickler syndrome (type I) present with early-onset cataract, open-angle glaucoma, myopia, degeneration of the vitreous, radial paravascular degeneration, lattice degeneration, retinal tear, and rhegmatogenous retinal detachment (Fig. 1). The classic findings on vitreous examination include an optically empty central vitreous with abnormal membranes posterior to the lens, in the peripheral vitreous, and over the pars plana. (Stickler syndrome type II can be clinically distinguished from type I by the presence of fibrillar or beaded vitreous.) Non-ocular findings of Stickler syndrome type I are variable and include midface hypoplasia, cleft palate, bifid uvula, hearing loss, and skeletal abnormalities/marfanoid habitus with early-onset arthritis (Fig. 2). Interestingly, patients with a premature stop codon located in exon 2 of COL2A1 have predominately the ocular phenotypes and lack many of the systemic findings typically seen with Stickler syndrome type I.

Diagnostics

Diagnosis of type I Stickler syndrome involves documenting the spectrum of ocular and non-ocular clinical findings associated with this systemic disorder. Genetic studies can help confirm a specific mutation but are not required to establish the diagnosis. All patients with a family history of Stickler syndrome should receive proper screening with slit lamp examination and dilated ophthalmoscopy with scleral depression.

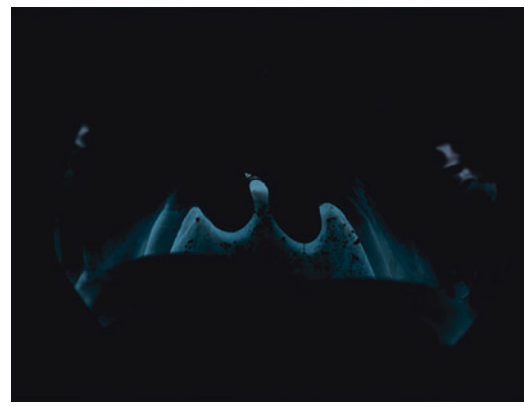
Differential Diagnosis

The differential diagnosis of Stickler syndrome (type I) includes other chondrodysplasias that can produce vitreoretinal abnormalities including type II Stickler syndrome, Marshall syndrome, Kniest dysplasia, Knobloch syndrome, and Weissenbacher-Zweymuller syndrome. Differentiating between these conditions is based on spectrum of systemic abnormalities and modes of inheritance.

Prophylaxis

Although no prevention exists for Stickler syndrome, prophylactic laser retinopexy can be considered for all areas of retinal breaks and lattice retinal degeneration in patients with Stickler syndrome to help reduce the risk for retinal detachment. Although the value of this treatment remains unclear, such intervention is not unreasonable given the 50% lifetime risk of retinal detachment in these patients.

Stickler Syndrome (Hereditary Progressive Arthro-Ophthalmopathy), Fig. 1 (Stickler syndrome cataract) Color photograph demonstrating early-onset cataract



Stickler Syndrome (Hereditary Progressive Arthro-Ophthalmopathy), Fig. 2 (Stickler syndrome bifid uvula) Color photograph demonstrating bifid uvula

Therapy

No cure is currently available for Stickler syndrome. Management involves preventing amblyopia, optically correcting for myopia, managing open-angle glaucoma, and treating retinal breaks and detachments.

Prognosis

The visual prognosis for Stickler syndrome is predominantly determined by the extent of vitreoretinal abnormalities and the subsequent risk of retinal detachment. Although visual prognosis with retinal detachments has improved following recent advances in surgical techniques, permanent vision loss is still possible in many cases due to recurrent retinal detachment. Other factors that influence visual prognosis include amblyopia, cataract formation, and development of open-angle glaucoma.

Epidemiology

Stickler syndrome (type I) occurs in approximately 1 in 7,500–9,000 neonates.

Cross-References

▶ Retina, Structure of

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Stickler Syndrome Membranous Vitreous Type

▶ Stickler Syndrome (Hereditary Progressive Arthro-Ophthalmopathy)

Stickler Syndrome Vitreous Type I

▶ Stickler Syndrome (Hereditary Progressive Arthro-Ophthalmopathy)

Stocker Line

▶ Iron Lines, Pterygium
▶ Iron, Corneal Deposits of

Stocker-Holt

▶ Juvenile Epithelial Dystrophy (Meesmann Dystrophy)

Strawberry Mark

▶ Port-Wine Stain (Nevus Flammeus)

Striate Keratitis

▶ Striate Keratopathy, Intraocular Surgery Causing

Striate Keratopathy, Intraocular Surgery Causing

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Synonyms

Striate keratitis

Definition

Focal intraoperative insult to the corneal endothelium results in posterior corneal edema and linear folds in Descemet membrane. Lines radiate to an incision and may be secondary to direct trauma from the phacoemulsification probe, bending of the cornea in intracapsular cataract surgery, or especially contact with lens substance in extracapsular cataract extraction, and is seen in almost half of such cases. Striate keratopathy generally resolves within 1 week.

Further Reading

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Striate Melanokeratosis

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Synonyms

Corneal pigmentary lines; Corneal verticillata; Pigmented epithelial lines

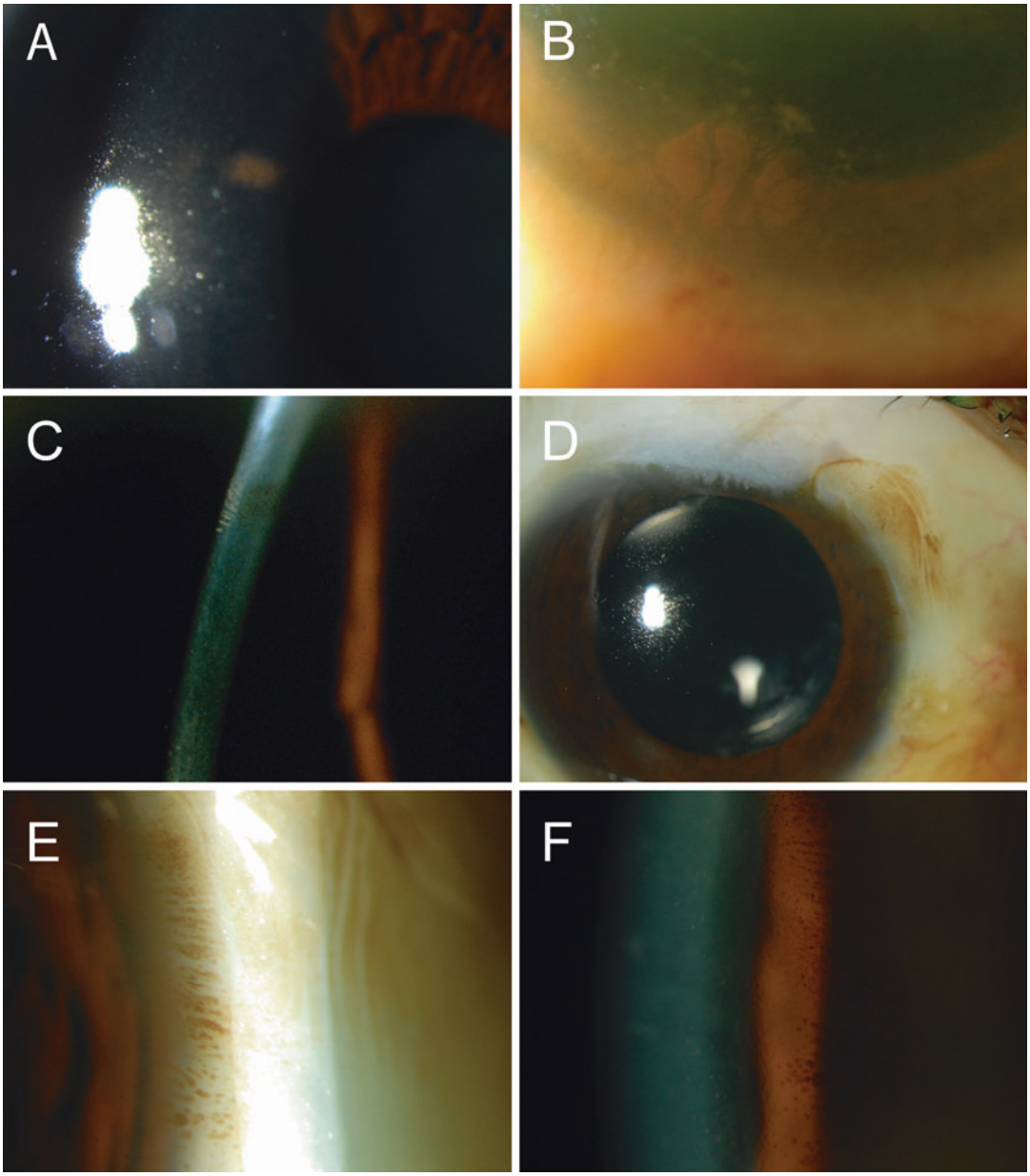
Definition

Striate melanokeratosis is a condition in which melanin-containing cells migrate centripetally along the subepithelial cornea, particularly in heavily pigmented individuals (Fig. 1a–c) (Boto-de-los-bueis et al. 2009). The corneal limbus contains a strip of melanoblasts containing pigment of varying density, depending on race. Individuals with dense perilimbal pigment will often demonstrate a benign migration under intact corneal epithelium, leading to a permanent local opacity. However, striate melanokeratosis may also be secondary to insult or chronic inflammation of the corneal epithelium. It has been postulated that melanin from local melanocytes transfers onto adjacent limbal epithelial cells, or the melanocytes themselves migrate centrally. This forms pigmented subepithelial lines, in some instances as part of a natural healing process in response to disruption of the corneal epithelium.

Histopathologic studies demonstrate melanin granules in the basal epithelium with occasional superficial scattering; the epithelium overlying remains intact and does not stain with fluorescein (Cowan 1964). The cornea, normally devoid of pigmented cells, assumes a vortex-shaped pattern of radiating lines extending from the limbus toward the apex 3–5 weeks after the inciting injury and may remain permanent or gradually fade. If substantial, cellular migration may even render the limbus unpigmented (Krachmer et al. 2010). While this process is typically benign and asymptomatic, the lesion may rarely be accompanied with impaired visual acuity (temporary or permanent), vascularization, and burning pain, the latter secondary to stimulation of corneal nerve endings by cell migration (Cowan 1964).

Etiology

Striate melanokeratosis typically manifests in dark-skinned individuals with markedly pigmented limbi in the abscess of corneal injury, but has been shown to occur secondary to disruption of corneal epithelium (especially within 4 mm of the limbus) such as diffuse superficial keratopathy, abrasion, recurrent corneal erosion, ulcerative keratitis, herpetic keratitis, neurotrophic keratitis, cataract surgery, and penetrating keratoplasty (Cowan 1964; Lemp 1991; Michaelson 1952; Stank



Striate Melanokeratosis, Fig. 1 Various presentations of striate melanokeratosis. (**a**) Striate melanokeratosis in heavily pigmented individual in paracentral cornea. (**b**) Peri-limbal pigment migration within peripheral cornea. (**c**) Pigment collection seen at the subepithelial cornea extending to corneal stroma. (**d**) Striate melanokeratosis in a post-trabeculectomy patient, low magnification. (**e**) Striate melanokeratosis in a post-trabeculectomy patient, high magnification. (**f**) Striate melanokeratosis in a post-trabeculectomy patient seen via retroillumination, high magnification

et al. 1990). In addition, 5-fluorouracil used during trabeculectomy has been observed to trigger pigmentary line formation in the cornea (Fig. 1d–f) (Krachmer et al. 2010; Peterson et al. 1990). This should not be surprising given that 5-fluorouracil has been demonstrated to stimulate pigment

formation in the skin with topical administration and in veins when used intravenously. Minor infiltration of pigmented cells (less than two millimeters) may also be seen with limbal nevus and melanoma (Cowan 1964).

Occurrence

Striate melanokeratosis is prevalent in heavily pigmented individuals with or without prior corneal epithelial injury. However, it has also been noted in Caucasians in cases of conjunctival melanosis, limbal nevus, and limbal melanoma.

Classification

Epithelial corneal degeneration
Corneal pigmentary lines

Cross-References

- ▶ Chloroquine Toxicity, Cornea Verticillata
- ▶ Corneal Limbus
- ▶ Primary Acquired Melanosis
- ▶ Stem Cells, Limbal, Corneal Epithelium Maintenance

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Stromal Bed

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Synonyms

Residual stromal bed (after ablation)

Basic Characteristics

The stromal bed is the part of the corneal stroma which is ablated with an excimer laser. In PRK, the stromal bed is exposed after Bowman's layer is ablated. In LASIK, the stromal bed is exposed after the flap is created and folded back. For a regular excimer laser ablation, it should be avoided to touch or hydrate the stromal bed prior to ablation. The remaining stroma after the ablation is referred to as the residual stromal bed (RSB). Only the RSB but not the flap stroma does contribute to the biomechanical strength of the cornea. Therefore, RSB thickness is an important parameter. The RSB thickness can be estimated by subtracting nominal flap thickness and ablation depth from total corneal thickness. More accurate is an intraoperative measurement by ultrasonic or OCT pachymetry (Wirbelauer and Pham 2004).

An intraoperative monitoring technique of stromal bed surface has been described but is not commercially available yet (Schruender et al. 2002).

Cross-References

- ▶ Corneal Stromal Haze
- ▶ Excimer Lasers

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Stromal Degenerations

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Synonyms

Keratoconus; Keratoglobus; Pellucid marginal degeneration (PMD)

Definition

Stromal degenerations of the cornea are characterized by bilateral, progressive thinning of the cornea.

1. Paracentral areas of the cornea in keratoconus
2. Peripheral thinning spherically in keratoglobus
3. Inferior and peripheral regions of the cornea in pellucid marginal degeneration

Epidemiology

Keratoconus is the most common corneal dystrophy/degeneration, while keratoglobus is rare. These degenerations are typically diagnosed in the second decade of life and progress into the third and fourth decades. Pellucid marginal degeneration is very rare.

Male and female distribution is roughly equal.

History

Patients with stromal degenerations can present both with stable and decreasing vision. Rarely, these patients may present with acute onset of pain and blurry vision in the setting of acute hydrops resulting from a break in Descemet's membrane.

Patients also sometimes complain of "ghost" images, or monocular polyopia. Often these visual aberrations cannot be corrected with spectacles. Patients may present after worsening irregular astigmatism having unsuccessfully tried spectacles and contact lenses.

Clinical Features

"Scissoring reflex" is evident on streak retinoscopy. Rizzuti's sign can be seen as a conical reflection of the nasal cornea when a penlight is shone from the temporal side. Munson's sign is seen as indentation of the lower eyelid when the patient looks down.

Slit-lamp exam demonstrates protrusion of the cornea paracentrally, inferiorly, or peripherally. Vogt's striae may be seen as vertical striations in the deep stroma or Descemet's membrane. The striae will disappear as pressure is applied to the cornea. A Fleischer ring may be seen in the epithelium as an iron deposit lines adjacent to areas of thinning.

Corneal topography exam will show thinning of the cornea with associated steepening also paracentrally, inferiorly, or peripherally.

Tests

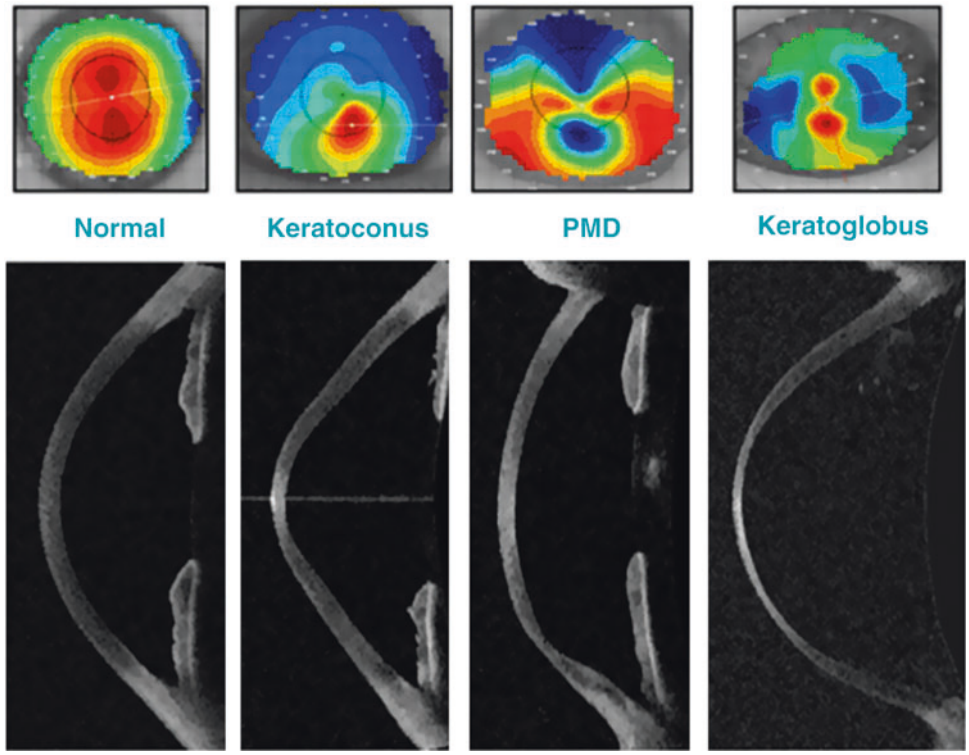
Corneal topography, manual keratometry, anterior segment optical coherence tomography (OCT), and pachymetry.

Differential Diagnosis

Contact lens induced corneal changes and corneal ectasia following refractive surgery.

Etiology

Etiology is unknown but they can be associated with collagen vascular disease, atopy, and Leber congenital amaurosis.



Stromal Degenerations, Fig. 1 Corneal tomography and corresponding anterior segment OCT in keratoconus, PMD, and keratoglobus

Treatment

Spectacles and contact lens may achieve suitable vision for the patient. Commonly, the patient will need a rigid gas permeable lens, or some type of hybrid contact lens to produce a hard central corneal surface.

Surgically, corneal collagen cross-linking with riboflavin and UV-A light has produced good results. Cross-linking restores mechanical strength to the corneal stroma and inhibits progression of the disease process.

Other surgical treatments include intrastromal corneal ring segments and radial keratotomy to flatten the corneal curvature in certain areas. End-stage surgical treatments include penetrating keratoplasty and deep anterior lamellar keratoplasty (Fig. 1).

Further Reading

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Stromal Dystrophies

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Synonyms

Amyloidosis V and familial amyloid polyneuropathy type IV (FAP-IV); Classic lattice

corneal dystrophy, LCD type 1 and Biber-Haab-Dimmer; Granular corneal dystrophy type 1 (GCD1), Groenouw corneal dystrophy type I; Granular corneal dystrophy type 2 (granular-lattice) (GCD2), Combined granular-lattice corneal dystrophy or Avellino corneal dystrophy; Lattice corneal dystrophy (LCD), gelsolin type (LCD2) Familial amyloidosis, Finnish type (FAF); Macular corneal dystrophy (MCD), Groenouw corneal dystrophy type II or Fehr spotted dystrophy; Meretoja syndrome

Definition

Corneal stromal dystrophies are a group of inherited disorders of the cornea that are caused by progressive accumulation of deposits within the stroma. These deposits are not caused by inflammation, infection, or trauma but by genetic mutations that lead to abnormal accumulation of insoluble material within the stroma. The disorders may or may not affect vision and can be symmetric or not. They usually present in the second to third decades of life. The major corneal stromal dystrophies include lattice, granular, and macular dystrophy.

Etiology

Stromal corneal dystrophies can be classified according to the presence or absence of the mutation in the transforming growth factor beta 1 (TGFB1) gene, located on chromosome 5q31. This gene encodes for keratoepithelin, a protein that is secreted by the corneal epithelium.

The TGFB1 dystrophies are granular, lattice, and Avellino. On the other hand, the non-TGFB1 dystrophies include macular dystrophy, Schnyder corneal dystrophy, congenital stromal corneal dystrophy, Fleck corneal dystrophy, central cloudy dystrophy of François, and pre-Descemet corneal dystrophy.

We will discuss here the most common three stromal dystrophies:

Lattice Stromal Dystrophy

Lattice corneal dystrophy (LCD) is the most common type of the corneal stromal dystrophies, and pattern of inheritance is autosomal dominant. There are five subtypes. LCD type 1 is the most frequent, which has been referred to as Biber-Haab-Dimmer corneal dystrophy. LCD type 2 is part of the systemic disorder familial amyloid polyneuropathy type 4 (Finnish type), also known as Meretoja's syndrome, and it is unrelated to the mutation of TGFBI protein. LCD types III and IIIA present later in life with thicker linear opacities in the mid-corneal stroma. LCD type III is an autosomal recessive condition presenting in the seventh to eight decade of life.

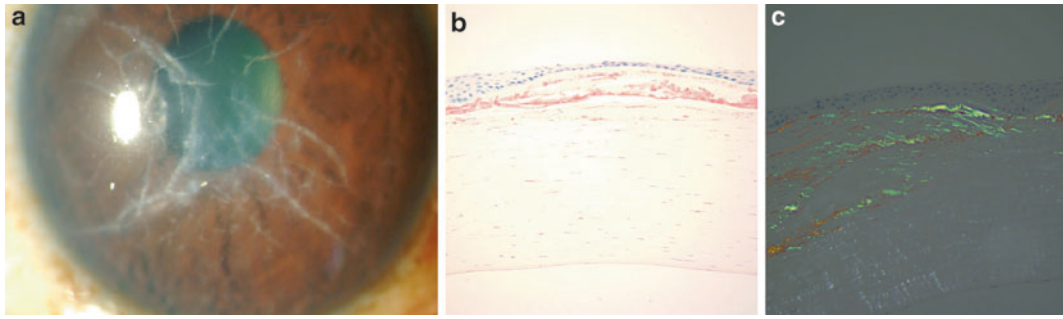
Clinically begins in the first decade and PK is indicated during the fourth or fifth decade. Recurrent epithelial erosions often occur. Stromal haze and epithelial surface irregularity may decrease vision.

On slit lamp, the opacities usually are most dense anterior and centrally, with a clear zone in the corneal periphery, characterized by lattice form of branching relucent lines in the corneal stroma (Fig. 1a). Histologically, corresponds to eosinophilic stromal deposits of amyloid that stain positive with Congo red (Fig. 1b) and show apple green birefringence with polarized light (Fig. 1c).

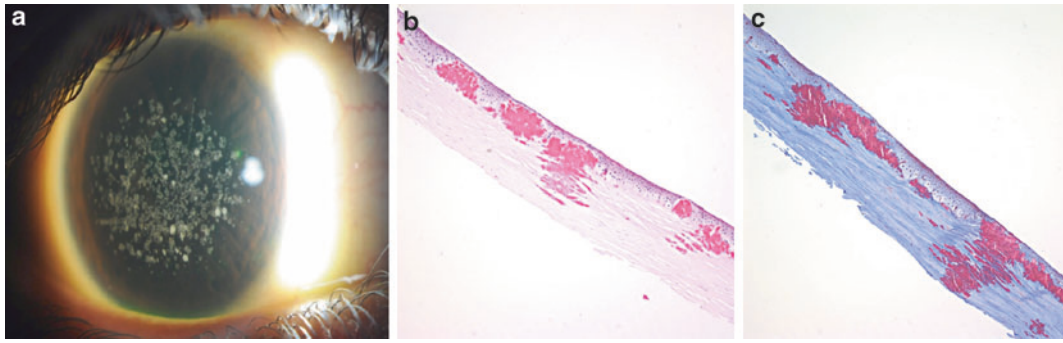
Granular Stromal Dystrophy

Granular corneal dystrophy (GCD) is an autosomal dominant condition also caused by mutations in the BIGH3 granular gene. There are two types of GCD including corneal dystrophy type I and granular corneal dystrophy type II (granular-lattice, Avellino corneal dystrophy).

GCD type I is the most common and benign entity of CSD. Clinically, most of patients are asymptomatic, whereas some others may develop recurrent erosions. Visual acuity remains stable because these opacities are separated by intervals of clear corneal stroma. Visual loss develops in the fifth decade of life or later. Slit-lamp examination is remarkable for the presence of well-demarcated opacities in the central stroma and intervening clear stroma (Fig. 2a).



Stromal Dystrophies, Fig. 1 (**a**) Clinical presentation. (**b**) Congo red. (**c**) Apple green birefringence



Stromal Dystrophies, Fig. 2 (**a**) Clinical presentation. (**b**) H&E. (**c**) Masson trichrome

Histopathologic findings with GCD type I show abnormal hyaline granular extracellular deposits within the stroma (Fig. 2b) that is highlighted by MT stains as chalky red stromal deposits (Fig. 2c).

GCD type II or Avellino dystrophy is a rare condition in which granular and lattice dystrophy components are present. The majority of patients with this condition are from Avellino region, in Italy.

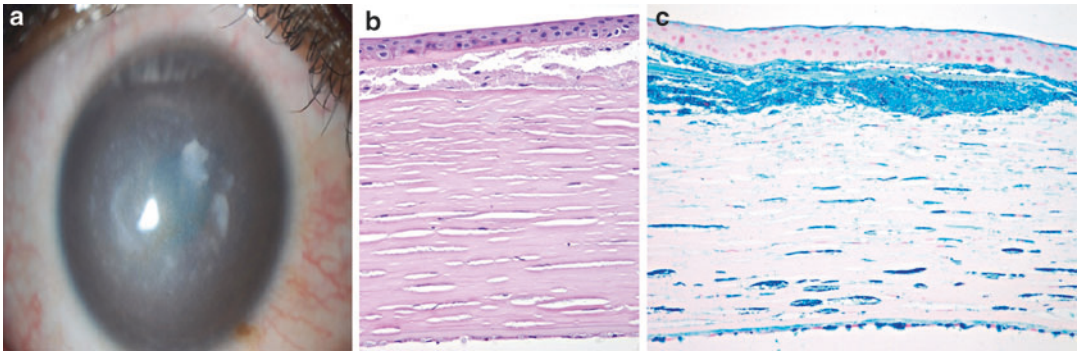
Histopathologically, stromal amyloid and hyaline deposits stain positive with Congo red and MT stains.

Macular Corneal Dystrophy

Macular corneal dystrophy (MCD) is an autosomal recessive condition caused by a mutation on chromosome 16, leading to a defect in the synthesis of keratan sulfate, the major glycosaminoglycan of the cornea. Although it is much less common than other main corneal stromal dystrophies, it is the most severe inherited disorder. MCD is relatively rare in the United States, but it is the most common stromal dystrophy in Iceland, due to its small gene pool, and in Saudi Arabia, due to frequency of consanguinity. There are three subtypes of MCD that have been described based on the presence or absence of immunoreactive keratan sulfate within various tissues.

Clinically, most of the patients develop severe visual loss by age 20–40 years and usually require corneal transplantation. On slit-lamp examination, the presence of a diffuse grayish indistinct stromal haze that extends from limbus to limbus, affecting all cornea layers, is noted (Fig. 3a).

Histopathologically, subepithelial extracellular deposits are highlighted by alcian blue stains (Fig. 3b) and colloidal iron stains (Fig. 3c), as well as intracellular abnormal mucopolysaccharide deposits in keratocytes and endothelial cells that demonstrate glycosaminoglycans.



Stromal Dystrophies, Fig. 3 (**a**) Clinical presentation. (**b**) Alcian *blue stain*. (**c**) Colloidal iron stain

Differential Diagnosis

Differential diagnoses for stromal dystrophies include:

- Epithelial and subepithelial dystrophies including epithelial basement membrane dystrophy, Meesmann corneal dystrophy, Lisch epithelial corneal dystrophy, and gelatinous drop-like corneal dystrophy
- Bowman's corneal dystrophies including Reis-Bücklers corneal dystrophy or Thiel-Behnke corneal dystrophy
- Endothelial corneal dystrophies including posterior polymorphous corneal dystrophy

Therapy

The treatment of corneal stromal dystrophies depends on the manifestation; if early in the disease process, no treatment is needed. Recurrent erosions can be treated with therapeutic contact lenses, superficial keratectomy, or PTK. When visual acuity is decreased, the phototherapeutic keratectomy, lamellar keratoplasty, or penetrating keratoplasty may be useful, depending on the depth of the corneal deposits.

In general, recurrence of any of these stromal dystrophies may occur also in the corneal graft. It is thought that lattice dystrophy recurs more often followed by granular and macular dystrophies.

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Stromal Graft Rejection

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Definition

Stromal graft rejection is a host immunologic response to donor corneal tissue characterized by inflammatory cells infiltrating the stroma. Rejection typically occurs months to years following a corneal transplant, but at minimum, the graft must be previously clear for 2 weeks after keratoplasty for the diagnosis to be made. Of the types of corneal graft rejection, isolated stromal rejection is less frequent than endothelial and epithelial rejection

and has fewer long-term consequences. It can be seen in conjunction with endothelial rejection.

Characteristic signs include peripheral haze or infiltrate that progresses toward the center of the graft. Stromal neovascularization may also be observed. In more severe cases of graft rejection, the stroma can become necrotic. Patients may complain of pain, redness, decreased visual acuity, irritation, or photophobia, but can often present asymptomatically.

In most cases, a good visual outcome is attained with prompt, aggressive treatment with corticosteroids to maintain integrity of the graft and minimize progression to the more severe endothelial rejection and graft failure.

Cross-References

► Endothelial Graft Rejection

Stromal Keratitis (Herpetic)

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Synonyms

Endothelial keratitis; Herpes simplex stromal keratitis (Yanoff et al. 2009)

Definition

Primary inflammatory condition of the corneal stroma caused by herpes simplex virus (Rapuano 2011).

Etiology

The most common cause of stromal keratitis is herpes simplex virus (HSV). HSV-1 typically infects areas above the waist such as the face, lips, and eyes. HSV-2 mainly affects the genital area but can be transmitted to eyes during birth or intercourse. Most cases of childhood stromal keratitis are caused by HSV-2 virus transmitted during birth (Kanski and Bowling 2003). In children, stromal keratitis is more frequently bilateral than in adults. It has also shown greater recurrence in children and greater visual loss (Finch 2010). Recurrence in HSV virus in adults is mediated by environmental factors such as fever, menstruation, sunlight, irradiation, and emotional stress (Yanoff et al. 2009).

Stromal keratitis is primarily an immune-mediated disease and can be but is not necessarily caused by active, replicating virus (Yanoff et al. 2009). Corneal antigens and HSV antigens cause a cell-mediated destruction process of the corneal stroma. Alterations of the antigenicity of the stromal keratocytes in which the virus lives can cause recurrent cycles of an immune-mediated or autoimmune inflammatory response. These antigens are expressed on means of antigen processing (MHC) molecules in corneal stromal cells and become the target of lymphocytes, CD4+ T cells, antiviral antibodies, serum complement, polymorphonuclear leukocytes (PMNs), and macrophages. The host immune response is necessary to destroy the virus that is present in the eye, but the detrimental effects of the immune response include inflammation and tissue destruction (Krachmer et al. 2010).

Clinical Presentation

There are two major types of stromal keratitis caused by HSV: necrotizing stromal keratitis and non-necrotizing stromal keratitis, also known as ► disciform keratitis or immune stromal keratitis.

Necrotizing Stromal Keratitis

This disease is usually a hypersensitivity reaction to live viral particles in the corneal stroma. It is characterized by necrotic, cheesy, stromal infiltration with stromal melting, accompanied by severe corneal opacification. Epithelial defects may be present; anterior uveitis with keratic precipitates may underlie the area of stromal infiltration, and intraocular pressure is usually elevated even with

minimal anterior chamber involvement. In its most severe form, the disease may cause scarring, vascularization, perforation, and lipid deposition. Common symptoms include redness, tearing, irritation, blurred vision, and photophobia (Kanski and Bowling 2003; Rapuano 2011). This condition can sometimes lead to glaucoma (Yanoff et al. 2009).

Non-necrotizing Stromal Keratitis

Non-necrotizing stromal keratitis typically manifests as diffuse or focal stromal opacities accompanied by a Wessely Ring (Yanoff et al. 2009). The epithelium and endothelium are usually spared. Common symptoms include redness, tearing, irritation, blurred vision, and photophobia. Anterior uveitis, elevated intraocular pressure, limbitis, folds in Descemet's membrane, and decrease in corneal sensation are also associated with stromal keratitis (Rapuano 2011).

Diagnostics

Clinical observation mediated by the use of a slit lamp can be used to make a diagnosis. Diagnosis can be confirmed by the use of polymerase chain reaction (PCR) to detect viral antigens. Examination of corneal scrapings can be used to identify the immune response against the corneal stroma (Krachmer et al. 2010).

Differential Diagnosis

Non-necrotizing Stromal Keratitis

Differential diagnoses of non-necrotizing stromal keratitis include herpes zoster disciform keratitis, ▶ Fuchs' dystrophy, acute corneal hydrops of ▶ keratoconus, or contact lens overwear (Rapuano 2011).

Necrotizing Stromal Keratitis

Differential diagnoses include primary or secondary bacterial or fungal keratitis and diseases that also present with an overlying epithelial defect. These conditions should be considered if there is a little response to antiviral medications (Rapuano 2011).

Prophylaxis

Long-term daily oral acyclovir reduces the rate of recurrence of stromal keratitis by about 50% and is usually well tolerated. This therapy should be considered in patients with recurrence only (Kanski and Bowling 2003).

Therapy

Treatment for both forms of stromal keratitis is generally the same, with a few additional measures for necrotizing stromal keratitis. Non-necrotizing stromal keratitis may resolve itself if the inflammation is mild, but in more severe cases, treatment is needed. Topical steroids such as prednisolone 1% in conjunction with antiviral prophylaxis are common treatment measures. Recommended dosing is four times per day at the start of therapy, then gradually tapered to once a week. Any epithelial lesions should be treated before beginning treatment with corticosteroids. In cases of necrotizing stromal keratitis, systemic antiviral medication (acyclovir 400 mg) five times a day for many weeks is indicated, especially to treat anterior uveitis. Corneal transplant is not recommended for cases of necrotizing stromal keratitis (Rapuano 2011).

Prognosis

Prognosis of non-necrotizing stromal keratitis is usually good, although some stromal scarring may occur and cause a reduction in vision. Prognosis of necrotizing stromal keratitis is somewhat poor since significant stromal scarring that can severely affect the vision remains. There is also a threat of recurrence of the disease (Rapuano 2011).

Epidemiology

Herpes simplex stromal keratitis is the most common cause for corneal opacification in the developed world. Around 500,000 patients in the United States are afflicted, with 50,000 episodes every year, and 20,000 new cases appearing every

year. Approximately 60% of corneal ulcers in developing countries are caused by herpes simplex virus, and as many as ten million people may have herpetic eye disease worldwide (Kanski and Bowling 2003). HSV establishes latency and can thus cause recurrent cases of stromal keratitis (Finch 2010; Krachmer et al. 2010).

Cross-References

- ▶ Disciform Keratitis, Herpes Simplex Virus Causing
- ▶ Fuchs Dystrophy
- ▶ Keratoconus

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Stromal Micropuncture, for Recurrent Corneal Erosions

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Synonyms

Corneal micropuncture; Epithelial reinforcement technique

Definition

An operative procedure where superficial puncture wounds are made in the cornea for treatment of recurrent erosion, map-dot-fingerprint dystrophy, and other superficial dystrophic or degenerative disorders of the cornea.

Indication

Patients with recurrent corneal erosions or epithelial basement membrane dystrophy (EBMD) that failed conservative medical management including lubricants, hypertonic saline solutions, topical corticosteroids, systemic tetracyclines, and therapeutic bandage contact lenses.

Contraindications

Patients with severe basement membrane dystrophy and numerous spontaneous, multifocal erosions are better candidates for superficial keratectomy than anterior stromal puncture. Patients with recurrent erosions or epithelial defects that are secondary to deeper corneal dystrophies or degenerations would not be good stromal puncture candidates. In these patients, the surgical management can vary from epithelial debridement for superficial disease to phototherapeutic keratectomy and anterior lamellar keratoplasty for stromal corneal pathology.

Techniques and Principles

Anterior stromal puncture is an in-office procedure generally done at the slit lamp after a careful exam for epithelial defects. Erosions and defects are best seen at the slit lamp using angled broad-beam illumination and retroillumination. Gentle pressure on the cornea may cause wrinkling indicative of loose epithelium.

Topical anesthetic and nonsteroidal drops are instilled preoperatively. A broad-spectrum antibiotic drop can be used preoperatively to reduce the chance of infection. Fluorescein can help aid in visualization of the erosions and puncture marks. A lid speculum can be used in a concerned patient.

The procedure can be performed using a specially designed 25-gauge needle with a bent top (preventing the patient from visualizing the tip and shaft) or a standard short 25-gauge needle attached to a tuberculin syringe. In the latter scenario, care must be taken to ensure that the punctures are made superficially. The clinician makes numerous superficial puncture wounds in the involved area. The punctures should not be confluent and should include 1–2 mm of normal epithelium outside the area of the defects. Treatment should be used with caution in the visual axis. Postoperatively, broad-spectrum antibiotic, nonsteroidal, and cycloplegic drops should be instilled. Some advocate for the use of a bandage contact lens after the procedure. Oral tablets for pain control can be useful. After the epithelium has healed, hypertonic drops should be used during the day and hypertonic ointments at night to promote epithelial integrity (Rubinfeld 1995).

While efficacious, the mechanism of action for anterior stromal puncture is not fully understood. The punctures are thought to produce a firm adhesion between the epithelium and the underlying stroma. This occurs through the epithelium filling the puncture sites forming a temporary adhesion, while normal attachment complexes can form (Hsu et al. 1993). Others postulate that the punctures induce a fibrotic reaction and a new basement membrane is formed. Histological studies have shown that the lesions produced by this procedure can indeed create subepithelial scars (Katsev et al. 1990).

Outcome

Reports of success after a single stromal puncture session for recurrent erosions are in the range of 80% (Reidy et al. 2000). The treatment may need to be repeated, usually because the initial area of treatment was inadequate. Significant scars are rarely visible for more than a few months after the procedure.

Complications

After anterior stromal puncture, patients can experience foreign body sensation as well as discomfort upon awakening. As with any corneal procedure, there is a rare chance of infection.

Cross-References

- ▶ Epithelial Basement Membrane Dystrophy
- ▶ Phototherapeutic Keratectomy
- ▶ Superficial Keratectomy

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Stye

- ▶ External Hordeolum (Stye)
- ▶ Hordeolum

Subacute Regional Lymphadenitis

- ▶ Cat Scratch Disease

Sub-brow Fat Pads

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Synonyms

Preseptal fat; Septal fat pannus; Submuscular fibroadipose tissue (SMFAT); Suborbicularis fibroadipose tissue

Definition

The sub-brow fat pad is a superficial fat layer existing between the orbicularis oculi muscle and orbital septum. It is a thin fat layer that is vastly spread in the upper eyelid just inferior to the orbital rim.

Structure

The sub-brow fat pad is a distinct layer of fibroadipose tissue that lies posterior to the orbicularis oculi and anterior to the orbital septum. Inferiorly, the sub-brow fat pad continues to the point where the orbital septum joins the levator aponeurosis, approximately 2–5 mm above the superior tarsal border (Meyer 1991; Kakizaki 2009). Superiorly and superolaterally, the sub-brow fat pad extends into the eyebrow region, where it is termed the "retro-orbicularis oculus fat" (ROOF).

The sub-brow fat pad contains more fiber components than the orbital fat pads. Histologic sections, gross dissections, and radiologic imaging have demonstrated that the fibrous septa within the fibroadipose tissue become contiguous with more compact lamellae of the orbital septum, giving the orbital septum a multilayered quality (Meyer 1991). The sub-brow fat pad is firmly attached to the orbital septum and cannot be completely dissected with blunt dissection.

Function

The physiologic significance of the sub-brow fat pad is to enhance eyelid and brow motility and to support the orbital septum.

Clinical Relevance

Over time, the sub-brow fat pad undergoes gravitational descent. Clinically, the displaced sub-brow fat pad can sometimes be confused with a prominent prolapsed preaponeurotic fat pad or a coexisting redundant eyelid fold. During blepharoplasty, the descended sub-brow fat pad must be addressed in addition to the skin/eyelid fat adjustment.

The anatomic relationship of the sub-brow fat pad and the eyelid must be remembered when operating on the eyelid, as the sub-brow fat pad can often be mistaken for the preaponeurotic fat of the eyelid and may lead to surgical error (Meyer 1991; Tan 2011).

In the Asian eyelid, there is often a more substantial sub-brow fat pad. Therefore, although ROOF resection alone is often efficacious in improving the thickness and heaviness of the upper eyelid in whites (Kakizaki 2009), it is often necessary to additionally resect the sub-brow fat pad in Asians to produce an aesthetic "double eyelid" (Ichinose 2008; Kakizaki 2009; Tan 2011).

In upper blepharoplasty procedures, volumizing the brow may result in a more aesthetically pleasing contour of the upper eyelid. If there is dermatochalasis due to deflation of the sub-brow fat pad, fat can be suctioned from a donor region (e.g., abdomen) and injected via cannula into the sub-brow fat pad region through the open blepharoplasty incision (Hoenig 2010).

Cross-References

- ▶ Levator
- ▶ Retro-Orbicularis Oculi Fat (ROOF)

References

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Subciliary Incision

► Transcutaneous Routes

Subciliary Incision, for Anterior Orbitotomy

► Infraciliary Blepharoplasty Incision, for Anterior Orbitotomy

Subconjunctival Hemorrhage

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Synonyms

Conjunctival hemorrhage; Hyposphagma

Definition

Subconjunctival hemorrhage (SCH) is a benign common clinical condition characterized by painless accumulation of blood underneath the conjunctiva or hemorrhage between conjunctiva and episclera in the absence of an obvious cause (Yanoff and Fine 2002; Tarlan and Kiratli 2013).

Etiology

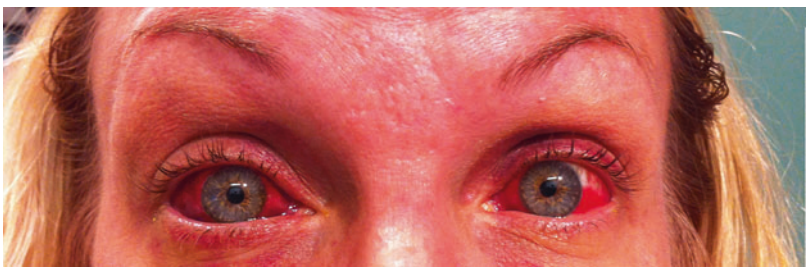
Most cases present suddenly without a clear cause. Contributing factors such as local trauma, acute hemorrhagic conjunctivitis, prolonged coughing, vomiting, or any other forceful Valsalva maneuvers have been previously described.

When SCH recurs, careful evaluation needs to be performed in order to assess association with systemic diseases such as diabetes mellitus, uncontrolled hypertension, and arteriosclerosis, any bleeding disorders including chronic therapy with anticoagulants, and, less commonly, ocular amyloidosis (Tarlan and Kiratli 2013).

There are ocular conditions that may also predispose to SCH. Besides any sort of globe rupture or orbital injury, conjunctivochalasis, contact lens wear, ocular surgery, and adnexal tumors can also be associated with SCH (Yanoff and Fine 2002; American Academy of Ophthalmology 2012; Sahinoglu-Keskek et al. 2013; Tarlan and Kiratli 2013).

Occurrence

SCH represents a relatively frequent eye entity and also a common emergency room diagnosis since its appearance can be dramatic and alarming to the patient (Fig. 1).



Subconjunctival Hemorrhage, Fig. 1 Bilateral subconjunctival hemorrhage

Classification

No classification has been documented for SCH.

References

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Subepithelial Corneal Degenerations

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Synonyms

Peripheral hypertrophic subepithelial corneal degeneration

Definition

Peripheral hypertrophic subepithelial corneal degeneration (PHSCD) is an idiopathic disorder that consists of peripheral, bilateral, elevated subepithelial corneal opacities, and adjacent abnormal limbal vasculature.

Etiology

The cause of PHSCD is unknown, though the lack of coexisting systemic or local ocular disease suggests that it is a primary condition. Similarities to familial pterygoid corneal dystrophy suggest that PHSCD may have a genetic component.

Clinical Presentation

PHSCD presents with peripheral, usually bilateral, symmetric elevated circumferential peripheral subepithelial corneal opacities (often sausage-roll shaped) and adjacent abnormal limbal vasculature. In most cases, the opacifications deform the normal shape of the cornea, leading to pronounced astigmatism. Some present with pseudopterygia. There is no chronic ocular surface inflammation. Symptoms include ocular surface discomfort (pain, itching, etc.) and reduced/blurred vision, though it can be asymptomatic (Maust and Raber 2003).

Diagnosis

PHSCD patients often present with decreased visual acuity due to astigmatism and ocular surface irritation caused by the irregular corneal surface and unstable tear film. Selected findings for the diagnosis of PHSD are (i) gray-colored continuous subepithelial fibrosis causing regular and irregular astigmatism, (ii) flattening of the cornea based on topography, and (iii) typical revascularization in the peripheral part of the fibrous tissue.

Differential Diagnosis

Idiopathic PHSCD, Salzmann nodular degeneration, familial pterygoid corneal dystrophy, corneal intraepithelial neoplasia, keratopathies, corneal amyloidosis, corneal keloid, hereditary hypertrophic scarring, and corneal trauma

Therapy

Asymptomatic patients do not require any treatment. Topical lubricants and superficial keratectomy can be used to relieve symptoms of ocular discomfort (Järventausta et al. 2014). Short-term recurrences after surgery are infrequent.

Prognosis

In the largest case study thus far (Gore et al. 2013), one-fourth of patients were asymptomatic and did not require any treatment. Conservative management with lubricants was sufficient for one-third of patients, and surgery was conducted in another one-third of patients who experienced significant ocular discomfort, progressive astigmatism, visual acuity changes, or neoplastic concerns.

Epidemiology

PHSCD was first described in 2003 and is a relatively new disease. It is uncommon and disproportionately affects white females, especially those with light-colored eyes.

Cross-References

- ▶ Corneal Degenerations
- ▶ Corneal Intraepithelial Neoplasia
- ▶ Salzmann Nodular Degeneration

References

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Subepithelial Graft Rejection

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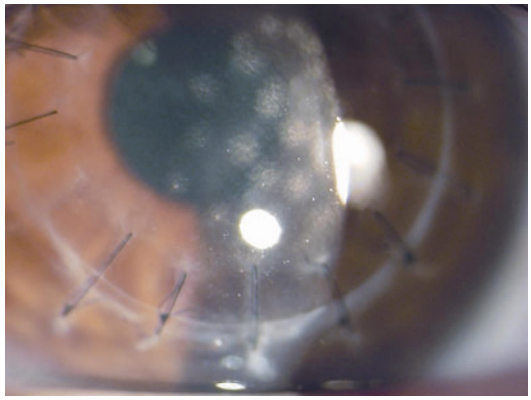
Synonyms

Allograft rejection; Subepithelial infiltrate

Definition

Subepithelial graft rejection refers to cellular infiltration of the cornea as discrete subepithelial infiltrates during allograft corneal graft rejection. These infiltrates are reminiscent of those seen in epidemic keratoconjunctivitis. They are small in size (0.2–0.5 mm) and hazy in color (white to grayish) and are usually scattered in the central cornea and occur exclusively in the donor tissue but not the peripheral recipient cornea. It could occur alone or in concert with attacks of epithelial or endothelial rejection (Copeland and Afshari 2013).

This phenomenon was first described by Krachmer and Alldredge in 1978 (Krachmer et al. 2011). These lesions are an early sign of acute allograft rejection and are considered to be harbinger of more intense reaction. They usually respond rapidly to topical steroid therapy and usually leave no residual infiltrate or scar. These infiltrates are usually seen early in the postoperative period (1–13 months). It seems that replacement of the epithelium with recipients' cells obviates its rejection in patients with older grafts. Symptoms include redness of the eye, decreased vision, light sensitivity, or discomfort in the eye that lasts longer than a few hours (Fig. 1).



Subepithelial Graft Rejection, Fig. 1 Subepithelial corneal graft rejection (Courtesy of Charles S. Bouchard, MD. American Academy of Ophthalmology, ONE Network Image Collection)

Etiology

Immunologic response of recipient cornea to antigens of donor cornea that occurred at the subepithelial layer of donor cornea.

Occurrence

Subepithelial graft rejection has occurred in 10–15% of cases of corneal graft rejection.

Classification

On the basis of anatomic location, corneal graft rejection could be classified as:

1. Epithelial
2. Subepithelial
3. Stromal
4. Endothelial

On the basis of locations for subepithelial infiltrates, they could be classified as:

Central and paracentral infiltrates. Where cellular infiltrates following subepithelial corneal graft rejection, acute adenoviral keratoconjunctivitis, protein-coated, extended-wear soft contact lenses and also after herpes simplex or zoster epithelial keratitis are classified in the central location (Krachmer et al. 2011).

Subepithelial infiltrates following marginal staphylococcal (catarrhal) keratitis and peripheral ulcerative keratitis (PUK) are located in paracentral or paralimbal zone (Copeland and Afshari 2013).

Cross-References

- ▶ Corneal Graft Rejection
- ▶ Peripheral Hypertrophic Subepithelial Corneal Degeneration
- ▶ Subepithelial Corneal Degenerations

References

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Subepithelial Infiltrate

- ▶ Subepithelial Graft Rejection

Submuscular Fibroadipose Tissue

- ▶ Retro-Orbicularis Oculi Fat (ROOF)

Submuscular Fibroadipose Tissue (SMFAT)

- ▶ Sub-brow Fat Pads

Suborbicularis Fibroadipose Tissue

- ▶ Retro-Orbicularis Oculi Fat (ROOF)
- ▶ Sub-brow Fat Pads

Subperiosteal Midface Lift

► Cheek Elevation, in Eyelid Repair

Subperiosteal Orbitotomy

► Extraperiosteal Route

Subretinal Exudation

► Subretinal Fluid

Subretinal Fluid

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Synonyms

Neurosensory retinal detachment; Serous detachment of the sensory retina; Subretinal exudation

Definition

Subretinal fluid corresponds to the accumulation of a clear or lipid-rich exudate (serous fluid) in the subretinal space, i.e., between the neurosensory retina (NSR) and the underlying retinal pigment epithelium (RPE), in the absence of retinal breaks, tears, or traction (Kanski et al. 2011). It represents a breakdown of the normal anatomical arrangement of the retina and its supporting tissues, i.e., the RPE, Bruch's membrane, and the choroid.

Etiology and Classification

Changes in choroidal flow, poor scleral outflow, breakdown of the RPE, and leakage/breakdown of normal or abnormal retinal vessels are the pathophysiological mechanisms that are isolated or in combination associated with subretinal fluid accumulation (Wolfensberger and Tufail 2000). There are some defining features, however, that are common to all cases of subretinal fluid: (1) serous fluid accumulation between the NSR and the RPE in the absence of a rhegmatogenous or tractional component; (2) a characteristic shifting of this fluid with postural changes; (3) a smooth, dome-shaped appearance of the detached retina lacking corrugations or fixed folds; and (4) the presence of associated local (ocular) or systemic conditions (Yanoff and Duker 2014). Identifying a precise etiology can be challenging since the causes of subretinal fluid accumulation are broad and heterogeneous, encompassing several ocular and systemic pathologies. For matters of systematization, an etiologic-based classification is portrayed here:

1. *Inflammatory and autoimmune diseases*: posterior scleritis, systemic lupus erythematosus, Wegener's granulomatosis, polyarteritis nodosa, relapsing polychondritis, dermatomyositis, Goodpasture's disease, rheumatoid arthritis, sarcoidosis, sympathetic ophthalmia, Vogt-Koyanagi-Harada disease, inflammatory bowel disease, pancreatitis
2. *Infectious diseases*: syphilis, toxoplasmosis, tuberculosis, Lyme disease, cat-scratch disease, cytomegalovirus infection, histoplasmosis, coccidiomycosis, cryptococcus, HIV infection
3. *Neoplastic disorders*: choroidal melanomas and nevi, retinal or choroidal hemangiomas, metastatic choroidal lesions, retinoblastoma, leukemia, multiple myeloma
4. *Vascular diseases*: diabetic retinopathy, retinal vein occlusions, retinal macroaneurysms,

hypertensive retinopathy, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, renal failure, eclampsia/preeclampsia

5. *Congenital abnormalities*: coat's disease, familial exudative vitreoretinopathy, retinal angiomatosis, optic pit, optic disk and/or retinal colobomas, morning glory syndrome, nanophthalmos
6. *Miscellaneous*: central serous chorioretinopathy, pathologic posterior vitreous detachment producing vitreomacular traction, epiretinal membrane, exudative age-related macular degeneration (AMD) (including neovascular phenotypes of AMD such as polypoid choroidal vasculopathy or retinal angiomatous proliferation), uveal effusion syndrome, iatrogenic (interferon or ribavirin treatment-related, among other dugs), bilateral diffuse uveal melanocytic proliferation (BDUMP)

Occurrence and Diagnosis

Unless precluded by hazy ocular media, the presence of subretinal fluid can generally be established during a thorough clinical examination using indirect ophthalmoscopy (Kanski et al. 2011). Even though the location, extent, and area occupied by the subretinal fluid can vary according to the etiology, the NSR detachment characteristically assumes a convex, dome-shaped configuration with a smooth, fold-free surface. Shifting of fluid to dependent positions with postural changes is a distinctive finding that should be sought during examination. Although the condition may be asymptomatic, decreased visual acuity can be manifest at presentation whenever the fluid accumulates under the macular area (e.g., central serous chorioretinopathy). Metamorphopsia, reduced color vision, and reduced contrast sensitivity are also commonly reported symptoms. The advent of leopard spots, consisting of scattered areas of subretinal clumping, may be seen after a prolonged NSR detachment has flattened (Yanoff and Duker 2014).

Subretinal fluid can be uni- or bilateral and may be observed as an isolate finding or occur in combination with other ocular findings such as lipidic exudation, retinal hemorrhages, serous and/or hemorrhagic retinal pigment epithelium detachments (PED), intraretinal fluid and/or cysts, choroidal neovascularization, choroidal effusion, cotton wool spots, or even optic nerve swelling. A detailed personal history along with a meticulous ophthalmologic examination in order to identify associated features is critical to establish a correct diagnosis. Sometimes the cause is readily apparent during fundus examination (e.g., choroidal tumor) but additional testing may be necessary depending on the clinical scenario (e.g., blood testing or even cerebrospinal fluid sampling when infectious or autoimmune etiologies are suspected).

Ancillary imaging like B-scan ultrasonography, computerized tomography, or magnetic resonance may be helpful in cases of hazy ocular media or retrobulbar pathology, whereas multimodal retinal imaging may assist in challenging cases (Kanski et al. 2011). With the advent of optical coherence tomography (OCT), the diagnosis of clinically asymptomatic serous elevations of the neurosensory retina has become more frequent. An optically empty space, filled with serous fluid, can be seen between the detached NSR and the RPE. OCT can be extremely valuable both in the differential diagnosis of subretinal fluid and in the monitoring of retinal changes during treatment (Yanoff and Duker 2014). Recently, advances in this imaging technique through enhanced depth imaging OCT (EDI-OCT) and swept-source OCT (SS-OCT) have been used to better evaluate choroidal changes in various diseases, such as central serous chorioretinopathy and Vogt-Koyanagi-Harada disease, thus enhancing our knowledge of the pathophysiological mechanisms involved. Fluorescein angiography (FA) and indocyanine green angiography (ICGA) can help differentiate various diseases, identify specific areas of leakage, and guide focal laser treatment and photodynamic therapy, when appropriate.

Differential Diagnosis

The differential diagnosis of subretinal fluid includes (1) serous or hemorrhagic PED, (2) tractional retinal detachment, (3) rhegmatogenous retinal detachment, (4) retinoschisis and/or foveoschisis, (5) intraretinal fluid accumulation (including cystoid macular edema), and (6) choroidal detachment (Wolfensberger and Tufail 2000). When a thorough fundoscopic examination is insufficient to establish the presence of a serous detachment of the sensory retina with a high degree of certainty, ancillary tests should be used to complement the clinical evaluation. This is especially significant in situations where treatment depends on the presence/absence of retinal/subretinal fluid (e.g., photodynamic therapy for chronic central serous retinopathy or focal laser treatment for focal diabetic macular edema). From all the available instruments, OCT is definitely the most widely used. It is a noninvasive diagnostic tool that provides insight into the retinal morphology through high-resolution, cross-sectional images of the retina. It can easily identify the precise location of fluid accumulation (intraretinal/subretinal/sub-RPE/choroid), thus being used both for diagnosis and follow-up.

Cross-References

- ▶ Optical Coherence Tomography
- ▶ Retinal Detachment
- ▶ Retinal Pigment Epithelium
- ▶ Retina, Structure of

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Subtenon's Anesthesia

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Synonyms

Episcleral anesthesia

Definition

Percutaneous application of anesthetics into the subtenon space between the globe and tendon capsule.

Epidemiology

Subtenon's anethesia (STA) is mainly used as an alternative to retrobulbar anethesia in less invasive ocular surgery. Usually it causes anesthesia but ineffective motorblock. Some surgeons use STA before intravitreal injection. It is also used in cataract surgery.

History

Subtenon's anesthesia has been used for a long time.

Clinical Features

STA does usually not produce sufficient motorblock. Therefore, the advantages over topical anesthesia are mainly the full anesthesia of the whole globe (Davison et al. 2007). For STA, there is mainly two techniques (Nouvellon et al. 2010). The first technique is the blunt technique, in which a small conjunctival incision is performed creating a conjunctival "button hole." Thereafter,

anesthetic is delivered into the subtenon space using a blunt needle. The second technique is performed using a small gauge sharp needle: After the plica semilunaris is punctured by a sharp needle, the needle is then pushed forward subconjunctivally towards the canthus into the subtenon space. Thereafter, the needle is pushed posterior forcing adduction of the globe and anesthetic is applied.

In both techniques, the anesthetic distributes in the subtenon space providing sufficient anesthesia of the whole globe. Using higher volumes, motorblock can be reached; however, at higher volumes, conjunctival edema is frequent.

Tests

Conjunctival edema has been shown to occur in 6–60%, and subconjunctival hemorrhage is found in 7–100%.

Differential Diagnosis

Topical anesthesia (TA), peribulbar anesthesia (PBA)

Etiology

The term "subtenon's anesthesia" is describing the location of the anesthetic in the subtenon space.

Treatment

See also "▶ Clinical Features."

Cross-References

- ▶ Anesthesia (Anesthetics), Local
- ▶ Cataract Surgery
- ▶ Peribulbar Anesthesia
- ▶ Retrobulbar Block
- ▶ Topical Anesthesia

References

Davison M, Padroni S, Bunce C, Rüschen H (2007) Sub--Tenon's anaesthesia versus topical anaesthesia for cataract surgery. Cochrane Database Syst Rev 18: CD006291

Nouvellon E, Cuvillon P, Ripart J (2010) Regional anesthesia and eye surgery. Anesthesiology 113:1236–1242

Sudoriferous Cyst

▶ Sweat Glands of Eyelid, Tumors Arising in

Sulfur Hexafluoride (SF6)

▶ Intraocular Gases

Sun Spots

▶ Lentigo Senile (Liver Spots)

Sunset Eye Sign

▶ Setting Sun Sign

Superficial Anterior Lamellar Keratoplasty (SALK)

▶ Lamellar Keratoplasty

Superficial Central Primary Degeneration Oleogutta

▶ Keratopathy Actinic (Labrador Keratopathy/ Spheroidal Degeneration)
▶ Keratinoid (Spheroidal) Degeneration
▶ Spheroidal Degeneration

Superficial Epithelial Keratectomy

► Superficial Keratectomy

Superficial Granular Corneal Dystrophy

► Reis-Bücklers Dystrophy

Superficial Keratectomy

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Synonyms

Superficial epithelial keratectomy

Definition

Operative procedure for treatment of recurrent erosion, map-dot-fingerprint dystrophy, and other superficial dystrophic or degenerative disorders of the cornea.

Epidemiology

No epidemiologic data available for this topic.

History

Superficial keratectomy has been performed since the early 1980s. Buxton et al. were among the first who performed this procedure to treat epithelial basement membrane dystrophy.

Clinical Features

See Treatment section below.

Tests

Thorough examination of the anterior segment with the slit lamp and corneal topography, pachymetry, and measurement of uncorrected and best spectacle-corrected visual acuity are mandatory to maintain best possible postoperative results.

Differential Diagnosis

Other types of incisional keratotomy:

- Phototherapeutic keratectomy
- Surface cautery
- Debridement
- Anterior stromal puncture

Etiology

See ► History section above.

Treatment

After topical anesthesia, the treated area is identified with fluorescein staining. The epithelium is then gently removed by scraping with a dry surgical sponge or a disposable blade. After the defined area is removed, the surface can be polished to receive best postoperative results. Finally, pressure patching is performed or the patient receives a therapeutic soft contact lens to assure appropriate wound healing and visual improvement.

Cross-References

► Phototherapeutic Keratectomy

Further Reading

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Superior Cantholysis

► Cantholysis

Superior Limbic Keratoconjunctivitis

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Synonyms

SLK; Theodore's superior limbic keratoconjunctivitis

Definition

SLK is a chronic noninfectious inflammatory disorder characterized by inflammation of the upper tarsal and bulbar conjunctiva. It was described by Frederick Theodore in 1963 as inflammation of tarsal and bulbar conjunctiva, punctate staining of the cornea and its adjacent conjunctiva, limbic proliferation, and presence of filaments limited to the superior limbus or upper fourth of the cornea.

Epidemiology

Superior limbic keratoconjunctivitis typically affects women with a female-to-male ratio of 3:1, usually affecting ages 20–60 years with a mean age of 50. There are no reported familial cases but it did affect identical twins. SLK affects people of different ethnic backgrounds and geographical distributions and not related to specific climates.

Etiology

The etiology of SLK is still to be determined as many studies were conducted and the causes are still unknown. Theories suspected a viral etiology but never have been proven. Whereas a bacterial cause has been excluded with negative cultures, no immunological-specific defect was found.

However, a number of associations were linked to SLK including dry eye disease, contact lens abuse, lid anomalies, and autoimmune diseases such as thyroid disease. Understanding the primary abnormality of the disease helps to explain many of these associations. In SLK there is continuous rubbing of the superior palpebral conjunctiva against the superior bulbar conjunctiva due to tight eyelids. This eventually leads to chronic inflammation and subsequently the clinical picture of SLK. Studies suggested that a mechanical factor was supported by the fact that there is upregulation of TGF-β2 and tenascin which are induced by mechanical trauma.

Based on this theory, several studies proved the association of SLK with thyroid dysfunction, particularly thyrotoxicosis, in which exophthalmos causes tightening of the eyelids which increases the friction between the palpebral and bulbar conjunctivae.

Furthermore, keratoconjunctivitis sicca (dry eye disease) is also associated with SLK. It occurs due to a deficiency in the tear film or tear component leading to a drying effect that causes friction between the upper lid and the bulbar conjunctiva, this causes inflammation of the palpebral conjunctival surface that prevents the normal healing process.

To summarize, there is no specific cause for SLK but a number of predisposing factors were proven, such as associated thyroid dysfunction (20–65%), autoimmune disease (3.5%), or contact

lens wear (10%). However, approximately 31.6% of cases are idiopathic or related to aging.

Clinical Presentation

SLK is a chronic disorder with flares and remissions. Typical symptoms may be unilateral or bilateral and include red eyes, foreign body sensation, pain, and tearing due to ocular irritation, mild photophobia, and frequent blinking. Some patients present with blepharospasm and mucoid discharge if filaments are present.

On examination, classical signs are (1) corneal hypoesthesia, (2) hyperemia and inflammation of the upper palpebral and bulbar conjunctivae, (3) fine papillary reaction, (4) sectoral injection, (5) thickening and redundancy of the superior bulbar and limbal conjunctiva (this is observed by having the patient look down and lifting the upper lid), (6) keratinization of the affected conjunctiva, (7) superior punctate epithelial keratitis, (9) and finally superior corneal and limbic filaments and thickening are frequently seen. In advanced cases, some patients present with ptosis and mucoid discharge.

Diagnosis

Diagnosis of SLK is mainly based on history and careful examination of the lid surface with lid eversion. Certain bedside tests can support the clinical diagnosis of SLK. With the use of topical anesthesia, sliding the superior bulbar conjunctiva over the superior cornea with a cotton-tip applicator, this shows the redundancy of the superior bulbar conjunctiva, as it is not seen in normal healthy eyes. In addition, the use of rose bengal or lissamine green stains will show coarse punctate staining of the superior bulbar and limbal conjunctiva, and the use of fluorescein dye clearly stains corneal epithelial defects such as punctate keratopathy. Cultures have no role, as no significant bacterial pathogen has been isolated. Histopathologically, the superior bulbar conjunctiva shows keratinized epithelium and polymorphonuclear leukocytes with an unusual pattern and aggregation of nuclear chromatin (pyknosis).

Differential Diagnosis

Using the clinical criteria in diagnosis, there are minimal differentials to SLK. Contact lens-induced keratoconjunctivitis mimics SLK in presentation and cytological characteristics but with lens intolerance and irritation. The use of thimerosal-preserved solution and superior riding of soft contact lens are suggested etiologies. The possible etiology of mechanical trauma behind the two could be the reason of similarity in presentation.

Contact lens-induced keratoconjunctivitis can be distinguished from SLK clinically as it occurs in younger patients, with no gender preference; could be unilateral, with greater corneal involvement and decreased vision, not associated with thyroid disease; and usually resolves upon discontinuation of use of contact lenses. Histopathologically, keratinization and filaments characterize SLK but are not as prominent in contact lens-induced keratoconjunctivitis. Therefore, the terminology contact lens-superior limbic keratoconjunctivitis (CL-SLK) is not precise to describe contact lens-induced keratoconjunctivitis and SLK cannot be used with contact lens consumers.

Other unlikely differentials are vernal and atopic keratoconjunctivitis which present with diffuse signs that are not confined to the superior limbus and tarsal conjunctiva as SLK. Also they are associated with seasonal recurrences and a history of atopy.

Prophylaxis

There are no definitive prophylactic therapies or recommendations to prevent the occurrence or relapse of SLK. However, some studies proved that after the combination use of 1% prednisolone acetate drops and 0.5% topical silver nitrate with the addition of 0.5% topical cyclosporine A four

times a day can give long-term (6 months–3 years) relief and improvement of signs and symptoms.

Therapy

Most patients will respond to lubricant eye drops, short course of topical corticosteroids eye drops, and mast cell stabilizers. Resistant cases may require additional treatment with autologous serum, bandage soft contact lenses, silver nitrate, thermocauterization, or others.

SLK is caused by mechanical trauma and dryness of the conjunctiva due to a defect in the tear volume and quality. Therefore, initial management of SLK includes the use of preservative-free artificial tears and lubricating ointments. Also application of mast cell stabilizers, such as lodoxamide tromethamine, cromolyn sodium, and ketotifen fumarate, has been proven to improve the symptoms of SLK.

Another treatment option is local application of 0.5–1% silver nitrate solution. It is applied to the palpebral or both the palpebral and affected superior bulbar conjunctiva. This causes chemical debridement which improves the symptoms for up to months. The use of solid nitrate should be avoided as it can cause serious chemical burn.

Different treatment modalities aim to reduce the mechanical interference between palpebral and bulbar conjunctiva. Patients who did not respond to silver nitrate and have normal Schirmer tear test and resection or recession of the conjunctiva serve best at improving symptoms. In cases with filaments, pressure patching or soft therapeutic contact lens could be used.

Permanent punctual occlusion can also be used in coexisting keratitis sicca with resolution of symptoms and findings including reversal of squamous metaplasia and increase in goblet cell number.

Several topical medications can help in the management of SLK. Topical steroids have significant effect in certain patients while vasoconstrictors only minimal. Vitamin A (retinol palmitate) eye drops are effective in 83% of users with no recurrence on continuation of use.

Cyclosporine A 0.5% can be used as primary or adjunctive therapy as immunosuppressant and immunomodulator that inhibits CD4, T-lymphocyte infiltration into lacrimal ducts, fibroblast proliferation, and collagen formation. It improves SLK symptoms by decreasing the inflammatory response and increasing tear production and may be effective in the management of SLK when treatment fails with topical corticosteroids.

Prognosis

Even though SLK is a chronic disease with remissions and relapses, with accurate diagnosis and management, it can be controlled. In general the prognosis of SLK is excellent because this disease is limited to the superior fourth of the cornea.

Cross-References

▶ Chronic Conjunctivitis

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Superior Ophthalmic Vein Thrombophlebitis

▶ Thrombophlebitis, of Orbital Vein

Superior or Inferior Altitudinal Visual Field Defects

► Altitudinal Visual Field Defects

Superior Orbital Fissure

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Definition

The superior orbital fissure is a foramen at the back of the orbit that separates the orbital roof from the lateral wall of the orbit and connects the orbit to the cavernous sinus in the brain.

Structure

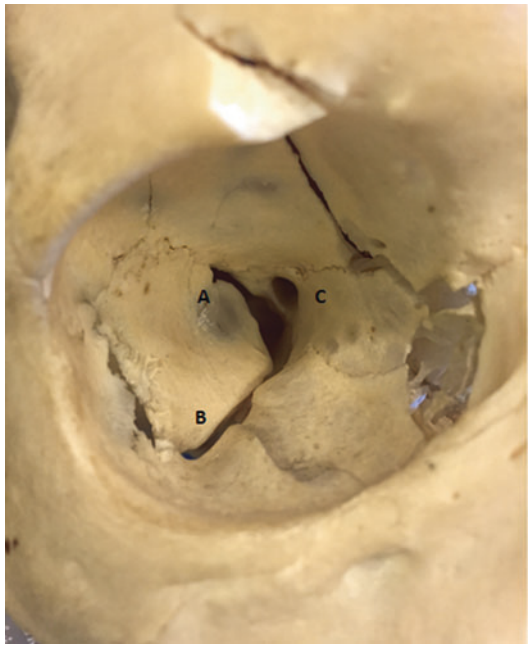
The superior orbital fissure divides the lesser and greater wing of the sphenoid bone and is closed laterally by the frontal bone. It is wider at the medial end and is therefore often described as comma shaped. It is roughly 22 mm long and the largest communication between the orbit and middle cranial fossa. The tip of the fissure is roughly 30–40 mm from the fronto-zygomatic suture. There are a number of very important structures that run through the superior orbital fissure. These include the superior and inferior divisions of the oculomotor nerve (III); trochlear nerve (IV); lacrimal, frontal, and nasociliary branches of the ophthalmic division of the trigeminal nerve (V1), the abducents nerve (VI), the superior and inferior divisions of the ophthalmic vein, and sympathetic fibers from the cavernous plexus. The optic foramen, through which the optic nerve and ophthalmic artery run, lies just superior and medial to the superior orbital fissure in the lesser wing of the sphenoid. It is separated by the optic strut. There is a common tendinous ring, also known as the annulus of Zinn, that spans the superior orbital fissure between the wide medial and narrow lateral parts and is comprised of the origins of the rectus muscles and the superior tendon of Lonckwood. The frontal nerve, lacrimal nerve, trochlear nerve, and superior ophthalmic vein pass above the annulus of Zinn; all other structures run through the annulus of Zinn. In general, nothing passes below the annulus, except rarely the inferior ophthalmic vein.

Function

The superior orbital fissure functions as a bony aperture through which many important structures pass from the brain into the orbit.

Clinical Relevance

Given the number of important cranial nerves and vasculature that passes through the superior orbital fissure, compromise in this area can present as diplopia, exophthalmos, and ptosis. Known as superior orbital fissure syndrome, this can occur in cases of infiltrative, inflammatory, or ischemic processes. A complete superior orbital fissure syndrome is defined as when all neurovascular components are damaged producing a total ophthalmoplegia, ptosis, and corneal hypoesthesia. The pupil may be dilated, miotic, or unreactive depending on the balance of parasympathetic and sympathetic damage. The superior ophthalmic vein may be dilated if obstructed giving rise to increase intraocular pressure, fullness of the upper eyelid, hyperemia of the deep Tenon's vessels, and retinal vein dilation. Differentiating between a lesion of the superior orbital fissure and anterior cavernous sinus cannot be done clinically and must be seen through imaging. Posterior cavernous sinus pathology can be differentiated by the presence of hypoesthesia in the cranial nerve V2 distribution. Superior orbital fissure syndrome and orbital apex syndrome can be distinguished by the presence of visual loss in orbital apex syndrome indicating compromise that includes the optic canal (Fig. 1).



Superior Orbital Fissure, Fig. 1 Anatomy of the orbital apex. (*A*) superior orbital fissure, (*B*) inferior orbital fissure, (*C*) optic canal

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Superior Transverse Ligament

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Synonyms

Whitnall's ligament

Definition

The primary suspensory support for the upper lid found at the intersection of the muscular and aponeurotic portions of the levator.

Structure

The superior transverse ligament (STL) is the transition point or fulcrum between the posterior muscular levator palpebrae superioris (LPS) and its anterior extension the levator aponeurosis (LA). The LPS originates in the orbital apex on the small wing of the sphenoid bone. It extends anteriorly to the orbital aperture where it is suspended from the STL. At this transition point to aponeurosis, it becomes thinner and fans out inferiorly in a sheet-like fashion. It extends horizontally forming the medial and lateral horns which attach to their respective canthi. Inferiorly, the LA attaches to the lower one third of the tarsal plate. The muscular portion of the levator is approximately 40 mm long, while the aponeurotic portion is approximately 14–20 mm in length.

Müller's muscle lies posterior to the levator aponeurosis. It extends from the superior border of Whitnall's ligament to where it inserts approximately 12 mm above the tarsal margin. The peripheral arcade runs along the surface of the muscle allowing for easier intraoperative identification.

The fibrous bands of the STL provide a hammock of support horizontally across the superior orbital aperture. Medially the STL attaches around the superior oblique tendon and trochlea. It extends laterally passing between the orbital and palpebral portions of the lacrimal gland to its lateral attachment approximately 10 mm above the lateral orbital tubercle (Whitnall's tubercle). The lateral orbital tubercle is adjacent to the superior oblique tendon. A few fibers also insert inferiorly at the lateral retinaculum.

Function

The superior transverse ligament (STL) was originally described by Whitnall in 1911. It is the

primary suspensory mechanism for the levator, upper eyelid, larcimal gland, and superior orbit. The STL is also the anatomic superior border of the upper eyelid and helps form the superior conjunctival fornix.

Given its location, the STL is responsible for the transition of the vector forces of the levator from anterior/posterior to the superior/inferior direction. Lockwood's ligament, found in the lower eyelid, is an analog to the STL (see "Retractors" and "Lower Eyelid").

Clinical Relevance

The levator and Müller's muscle are the two retractors of the upper eyelid. Disinsertion, dehiscence, abnormalities of the muscle, or lesions affecting these muscles can cause blepharoptosis or lid retraction. Blepharoptosis surgery is one of the most common oculoplastic procedures thus making identification in the operating room crucial.

The STL's location adjacent to the LPS and function as the primary suspensory mechanism of the upper lid make it an important landmark in surgery. Anatomically, it is often easily identified as white fibrous bands surrounding the levator (Lim et al. 2009). Structural differences in the STL of individuals may affect the eyelid structure and appearance which can impact the success of surgical results.

Weakening of the STL with aging or trauma has also been shown to decrease the ability to elevate the eyelid thus contributing to ptosis.

Cross-References

► Retractors, Lower Eyelid
► Iris Retractor

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Supplementary Pseudophakic IOL

► Piggyback Intraocular Lens

Suprasellar Mass Lesions

► Chiasmal Disorders

Surface Anesthesia

► Topical Anesthesia in Eye Surgery

Surface-Wrinkling Maculopathy

► Cellophane Maculopathy

Surgical Approaches

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Introduction

The most significant improvement in glaucoma surgery over the past 10 years is the transition to safer, more physiologic outflow procedures. These

newer blebless procedures lower IOP by reducing resistance to flow through natural trabecular or uveoscleral pathways and are easily combined with phacoemulsification. From a canal-based perspective, procedures such as iStent (Glaukos Corp, Laguna Hills, CA, USA), trabectome (NeoMedix Corporation, Tustin, CA, USA), canaloplasty (iScience Ellex, Menlo Park, CA), gonioscopy-assisted transluminal trabeculotomy (GATT), Kahook Dual Blade (KDB) (New World Medical, Rancho Cucamonga, California, USA), and Hydrus Microstent (Ivantis, Inc., Irvine, CA) likely provide the most long-term benefit to patients with early open-angle glaucoma before their natural collector channels undergo severe atrophy and develop a diminished ability to drain aqueous adequately (Nesterov et al. 1974; Fellman et al. 2015).

This may also be true for the newly approved supraciliary devices (Vold et al. 2016) aimed at reducing IOP by enhancing uveoscleral outflow. In addition, FDA trials involving less-invasive filtration procedures are promising as these newer techniques attempt to standardize filtration and offer safer methods to achieve external filtration (Sheybani et al. 2015; Batlle et al. 2016).

Although we are unable to visualize the improvement in aqueous flow into the collector channels postoperatively (Fellman 2014), one may be able to assess flow into the collector channels intraoperatively following canal-based surgeries (Fellman and Grover 2012). This inability to assess the surgical success postoperatively (aside from intraocular pressure) is very different than our experience with a filtering surgery. With a trabeculectomy, the bleb morphology can often help confirm a successful or failed surgery. When a canal-based surgery fails, we have a limited ability to determine why or how failure occurred.

Fortunately, over the past several decades, refinements in wound healing for trabeculectomy have improved filtration surgery (i.e., mitomycin C and 5-FU). To date, the authors know of no research or information on modulating wound healing within the anterior chamber angle following canal-based surgeries. Once wound healing in the canal can be modulated, the authors postulate that canal-based surgery will be even more successful and popular.

When one cannot maximize the patient's inherent trabecular or uveoscleral drainage system, a new drainage system must be created. The two most common glaucoma surgeries in which a new artificial drain is created are trabeculectomy and glaucoma drainage implants. Successful trabeculectomy creates a filtering bleb, which represents drainage of aqueous through a partial-thickness scleral flap into the subconjunctival and sub-tenon's space. Drainage implants use a tube to shunt aqueous from within the eye to a reservoir sutured to the sclera, beneath Tenon's capsule and conjunctiva. This chapter will further discuss these two main glaucoma surgeries as well as provide an overview of other less-invasive surgical procedures and their indications.

Philosophical Considerations on the Approach to a Surgical Glaucoma Patient

The decision for glaucoma surgery must always be made in conjunction with an understanding of what long-range IOP is necessary to prevent glaucomatous visual loss. This requires considerable experience. The more likely the patient is to lose vision during their lifetime due to uncontrolled glaucoma, the more likely the patient should have aggressive IOP control. Both the physician and patient should be cognizant of the important role incisional glaucoma surgery plays in reducing vision loss from glaucoma. Progressive VF loss is more likely to occur in advanced disease, especially without a significant reduction in IOP (Musch et al. 2009). Under these circumstances, the risks associated with significant IOP reduction are warranted. The physician must clearly explain the potential benefits and complications of the anticipated surgery with the full expectation of what needs to be accomplished and what to do if the surgery fails. To paraphrase George Spaeth MD "there must be a certainty when considering glaucoma surgery, that the person will become significantly worse in the absence of surgery." This is because glaucoma surgery, especially in patients with multiple risk factors for complications and or failure, is not

Surgical Approaches, Table 1 Factors in determining canal-based versus subconjunctival drainage of aqueous

Deciding factors	Canal-based (iStent, trabectome, canaloplasty, trabeculotomy, KDB) GATT	Subconjunctival surgery Filtration or tube shunt
Gonioscopy and angle	Angle must be open with clear landmarks, scleral spur delineated	Angle may be open or closed
Disk damage	Mild to moderate disk damage	Any level of disk damage, typically advanced
Risk	Lower risk surgery	Higher risk surgery (short and long term)
Age	Younger patients are better candidates because the collector system is less atrophic	Any age
Medication tolerability	Postoperative patients more likely to still require medications	Best for patients intolerant to medical therapy
Prior ALT	ALT may cause scarring in canal	Subconjunctival filtration not dependent on prior ALT
Ocular discomfort	Rare	More common with dysesthesia, tearing, potential diplopia, tube exposure, etc.

always successful, and a significant complication may further reduce vision. It is incumbent upon the physician to minimize surgical risk by choosing the best procedure for the unique circumstances for the patient (Table 1).

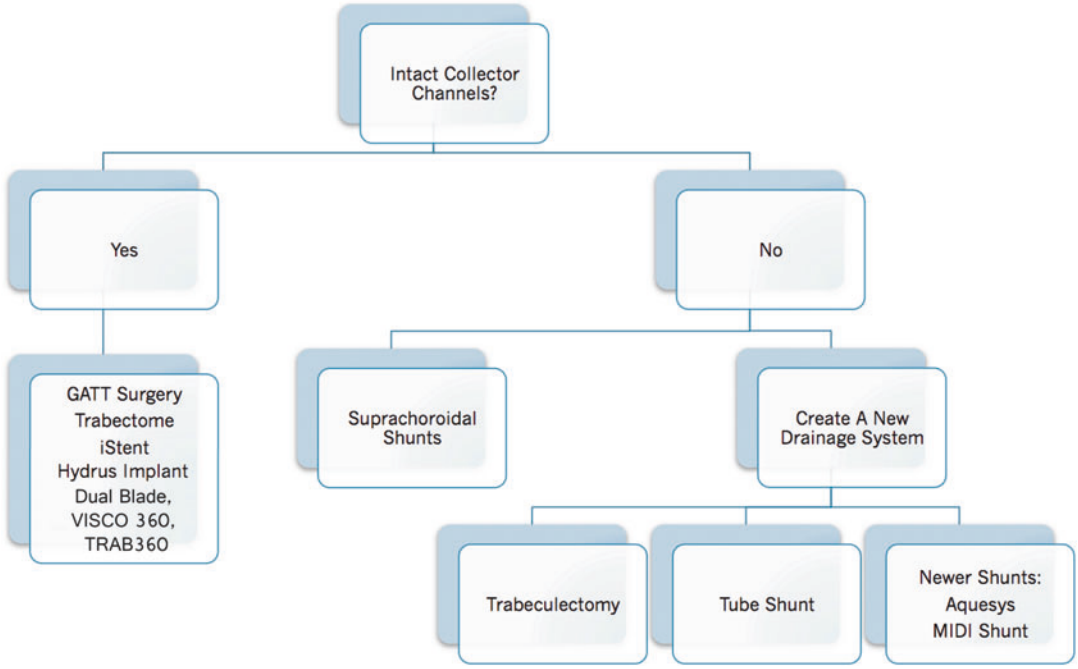
Glaucoma patients must understand that elevated IOP leads to visual loss and that in spite of our best efforts, glaucomatous visual loss may occur during their lifetime (Malihi et al. 2014) and that preventing blindness from glaucoma is an uphill battle. Communication between physician, patient, and family is crucial when dealing with the highly variable outcomes of glaucoma surgery that are mainly due to unpredictable wound healing and the intricacies of this unrelenting disease. The authors stress that the key to the surgical approach is to tailor the procedure to the patient's unique needs and disease state, not simply fall back, as in years past, on filtration or tube-shunt surgery for every patient. As we learn more about uveoscleral outflow, preserving collector channels and modulating wound healing in the canal, outcomes for improving natural channel outflow will improve, much like it has for filtration surgery over the past decades.

Preliminary Assessment of the Glaucoma Patient

Decades ago, most patients with uncontrolled primary open-angle glaucoma (POAG) or primary angle-closure glaucoma (PACG) underwent filtration surgery. Today, many surgeons prefer drainage implants over filters because no limbal bleb is present, but these devices still share many problems of external filtration including hypotony, scarring, and other unique problems such as diplopia and tube and plate erosion. Both of these time-honored procedures divert the aqueous underneath the conjunctiva creating an artificial drainage space. Today, patients now have a choice between improving flow into their natural drain and creating a new one (Fig. 1). A great deal of clinical experience is necessary in order to decide on the best surgical procedure for the glaucoma patient. The preliminary clinical assessment is the key to deciding what is best; the mnemonic A, B, C, D, and E is useful in the decision-making process.

(A) **Angle and age**

- Angle. It is imperative to assess the angle gonioscopically in order to diagnose the type of glaucoma and view the potential structures for canal-based surgery. If the surgeon is unable to locate the scleral spur, then the angle anatomy may not be favorable for a stent or canal procedure. If the angle structures are easy to identify, consider a canal procedure, especially if the desired IOP is in the mid-teens and the optic disk has mild to moderate damage. Explain to the patient that if flow



Surgical Approaches, Fig. 1 Decision tree for micro-invasive glaucoma surgery versus subconjunctival artificial drainage. Once the technology to visualize the native collector system is available, this decision tree will prove most useful to either enhance resident flow or create a new drainage system

does not improve through their natural collectors, they will need a more invasive procedure to create a new drainage system.

- Age. A also stands for age because younger patients likely have a more intact resident outflow collector system that can be revived compared to a patient who has been on topical glaucoma medications for 30 years with a more atrophic downstream collector system.

(B) **Blood aqueous barrier.** The condition of the aqueous should be evaluated prior to glaucoma surgery. Preoperative flare and cell are signs of a damaged blood aqueous barrier (BAB). A damaged BAB may result in an abnormally high amount of inflammation postoperatively and therefore must be detected preoperatively as this will affect the surgical decision process. For example, the success rates for trabeculectomy and many angle-based surgeries are highly dependent on a pristine blood aqueous barrier. Consider a drainage implant or possibly a trabeculotomy in patients with a permanently altered BAB.

(C) **Conjunctiva.** The condition of the conjunctiva is critical to the success of filtration surgery. If the patient has scarring of the conjunctiva or terrible ocular surface disease, consider a different procedure such as a drainage implant. Often, the health of the conjunctiva can also provide insight into the downstream collector system. If the conjunctiva is severely scarred, or scleral staphyloma is widespread, it is likely that the inherent collector system is dysfunctional.

(D) **Disk**. The stage of glaucoma exemplified by disk and field damage is critical in deciding on an appropriate glaucoma procedure. For example, if the patient has advanced disk damage, or is unable to tolerate drops, a trabeculectomy is ideal to blunt an IOP spike postoperatively and achieve long-term IOP reduction with minimal drug therapy. Under these circumstances, the risk of

blebitis and a lifetime of bleb vigilance are worth the risk of bleb-related visual loss.

(E) **Expertise.** When deciding on a new procedure, it is critical to find the optimal initial procedure. Consider the ABCDEs as a method to determine the best initial procedure for your patient. The overall most important decision is what is best for the patient in the hands of their surgeon. Many of these new minimally invasive surgeries have a steep learning curve and are not without risks.

In general, trabeculectomy lowers IOP more than a canal procedure and is mainly reserved for patients with advanced disease who require very low IOPs in order to maintain their vision. The newer MIGS procedures are finding their place in patients that require combined cataract-glaucoma procedures who have mild to moderate disk damage who may fare well with an IOP in the mid-teens. Typically, MIGS will not get the IOP below episcleral-venous pressure, which is usually close to 10 mm Hg.

This chapter will discuss incisional glaucoma surgery using an outline based on Fig. 1. First, we will discuss surgical procedures that are designed to enhance a patient's inherent drainage system. We will then proceed to discuss more invasive surgical procedures that are designed to create a new drainage system. Lastly, we will discuss surgical procedures designed to decrease aqueous production.

Overview of Incisional Glaucoma Surgeries That Enhance Drainage Through the Resident Venous Collector System (Trabecular Schlemm's Canal Episcleral Network)

Procedures

Trabeculotomy,

- 360° circumferential trabeculectomy, *ab externo*
- 360° circumferential trabeculotomy, *ab interno*, gonioscopy-assisted transluminal trabeculotomy (GATT)
- Trabectome, partial circumference *ab interno* trabeculotomy
- Kahook Dual Blade (KDB)

Mechanism of Action

Trabeculotomy cleaves open the trabecular meshwork and thereby improves flow into Schlemm's canal and resident collector channels. Following this surgery, aqueous no longer needs to travel through the trabecular meshwork juxtacanalicular tissue in order to gain access to the collector channels. *Ab externo* implies a limbal incision with scleral dissection to find the canal, while *ab interno* means that the canal is approached through the anterior chamber without conjunctival or scleral incisions, a major benefit if filtration surgery is ever needed.

Indications/Contraindications

Indications Open-angle glaucomas that are classified as mild to moderate. This surgery works best in glaucoma where the trabecular meshwork is likely the site of pathology, such as pseudoexfoliation glaucoma, developmental glaucoma, POAG, and steroid-induced glaucoma. Surprisingly, circumferential trabeculotomy is also effective in patients with failed filtration and tube-shunt surgery with open angles. Patients who have undergone several anti-VEGF intravitreal injections and develop subsequent glaucoma also do well with this surgery.

Contraindications Advanced glaucoma, closed-angle glaucoma, an inability to view the anterior chamber angle (except with external approach), a patient at high risk for snuff out if there were an IOP spike in the postoperative period, pseudophakia with advanced disease, and/or an unstable intraocular lens.

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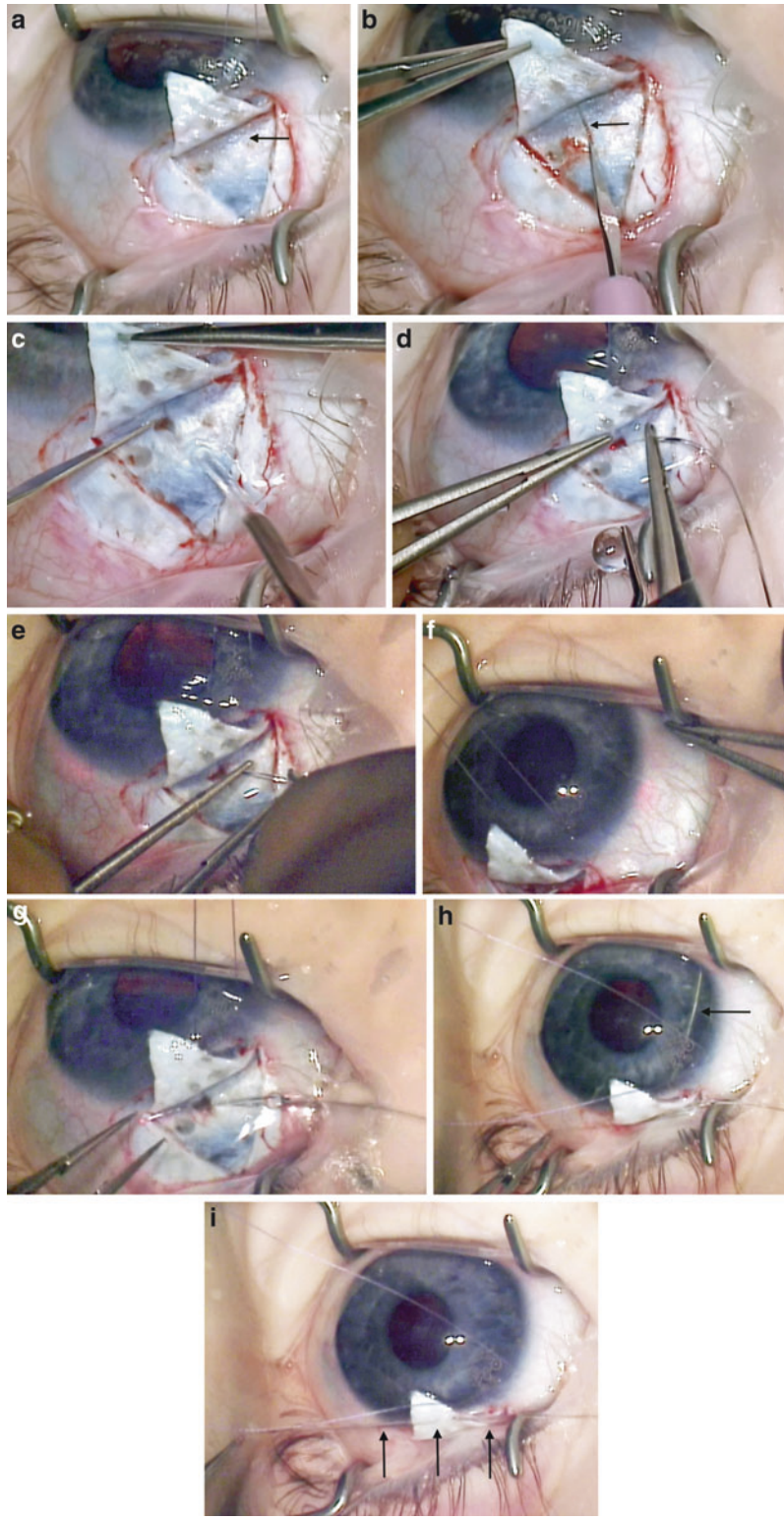
Key Procedural Components

360° Circumferential Trabeculotomy: *Ab Externo* (Fig. 2)

- Create a large scleral flap, and dissect it anteriorly into the cornea so that one can identify the scleral spur, a white circumferential band in the scleral bed (Fellman 2003).



Surgical Approaches, Fig. 2 (continued)

- Make a radial incision across the spur dissecting into the sclera, fiber by fiber, until the roof of the canal is penetrated, while avoiding entering the anterior chamber. Then make a T-shaped incision along the canal.
- Externally cannulate Schlemm's canal with either a 6.0 blunted Prolene suture or a micro-catheter and pass for 360°. If using a lighted micro-catheter, one can watch the beacon of light tip progress circumferentially along the canal. If using a suture, be sure to premeasure the suture so one knows when to expect to see the distal end. Keep in mind that the average circumference of Schlemm's canal is slightly under 4 cm.
- After retrieving the distal end, tension is placed on both sides of the suture and the 360° trabeculotomy is created. After washing out the hyphema, close the scleral flap and the conjunctiva in a watertight fashion.

GATT Procedure: 360° Circumferential Trabeculotomy: Ab Interno (Fig. 3)

- A cohesive viscoelastic is used to inflate the anterior chamber.
- A goniotomy is created in the nasal quadrant through a temporal corneal paracentesis. A suture (5-0 prolene suture with a small blunted tip) or lighted micro-catheter is passed through a superior or inferior paracentesis. Within the eye, the catheter/suture is used to cannulate Schlemm's canal and pass it around the canal 360°.
- The distal aspect of the catheter/suture is retrieved and externalized, thus creating a 360° trabeculotomy without limbal dissection.
- The viscoelastic is washed from the anterior chamber along with the resulting hyphema.

Trabectome (Fig. 4)

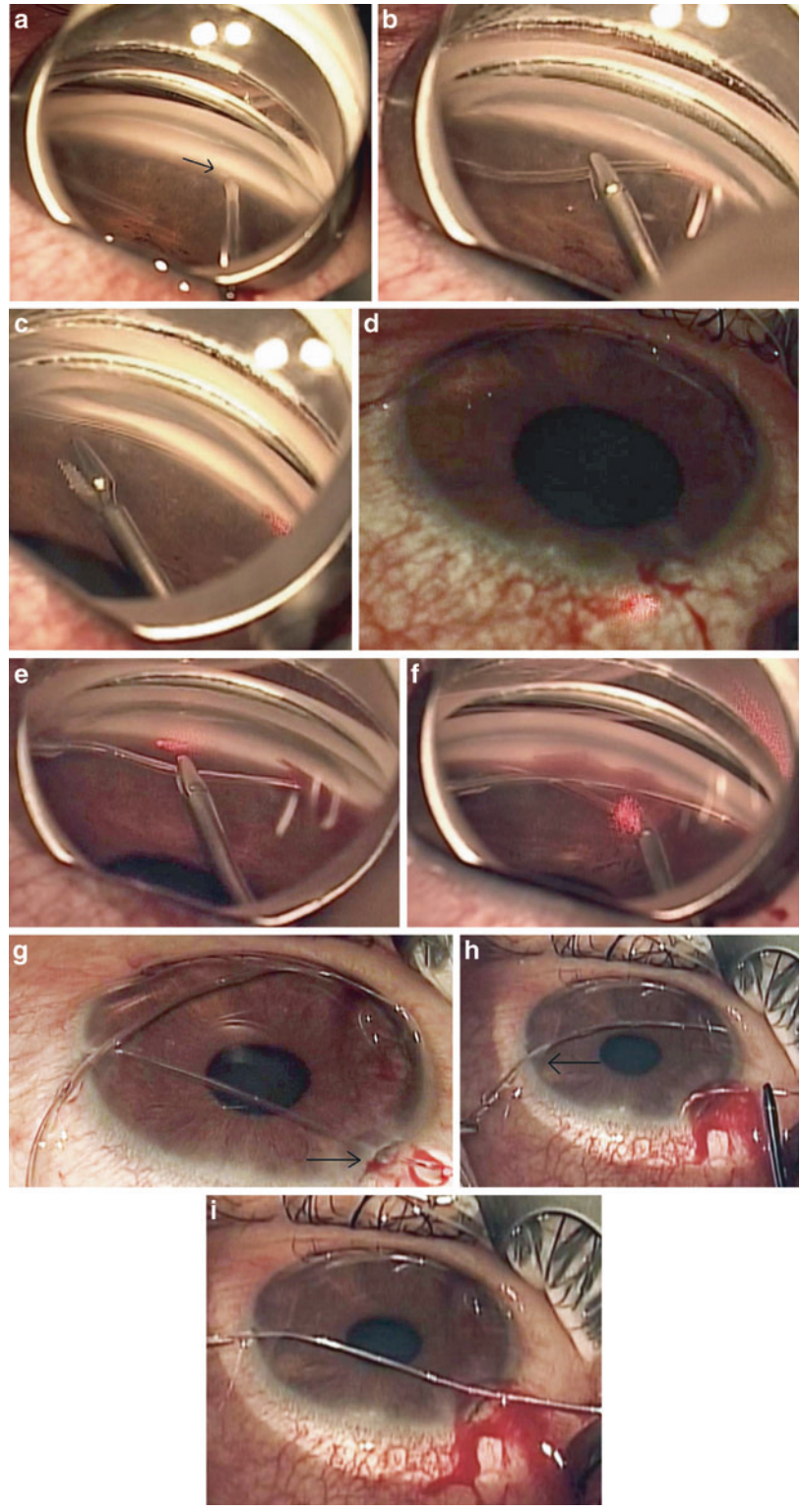
- A temporal clear corneal incision is created.
- The head is tilted away from the surgeon, and microscope tilted toward the surgeon.
- The trabectome handpiece is inserted into the anterior chamber after the irrigation is activated.
- A goniolens is placed on the eye, and the handpiece is directed into the nasal quadrant.
- The trabecular meshwork is incised with the tip of the handpiece. Electrosurgery is foot pedal activated which ablates the trabecular meshwork and inner wall of Schlemm's canal for typically a 4–5 clock hour arc.

Kahook Dual Blade

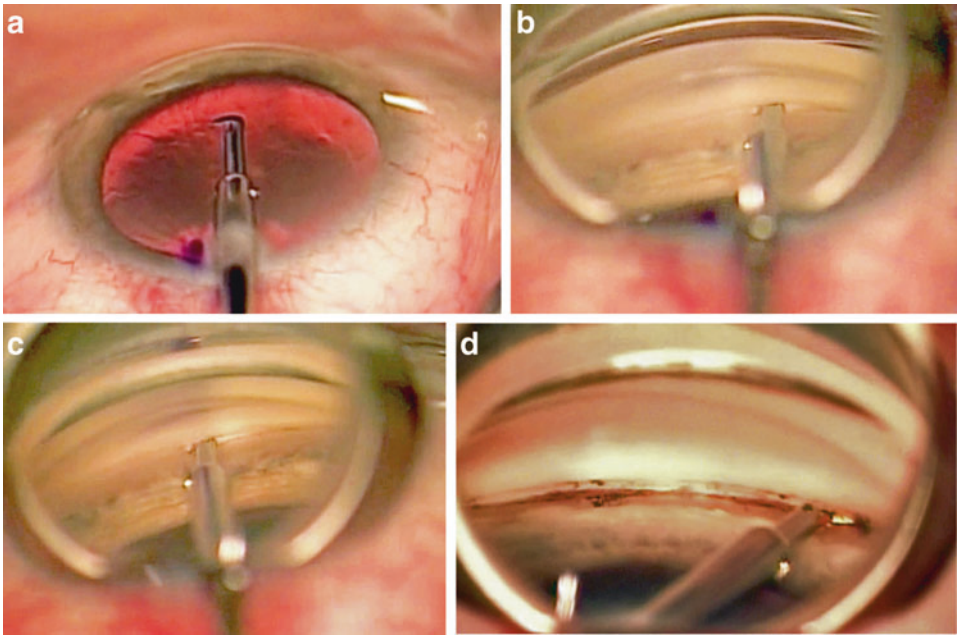
- Similar approach as the trabectome with the exception that the KDB manually incises the trabecular tissue, whereas the trabectome surgery uses electrosurgery.
- KDB requires only a blade and does not require the irrigating setup that is required by trabectome. However, the KDB is performed with the aid of an intracameral viscoelastic which is washed out at the end of the procedure.

S

Surgical Approaches, Fig. 2 Trabeculotomy *ab externo*. (**a**) Following a large conjunctival peritomy and the creation of a 70% thickness scleral flap, one can appreciate the scleral spur (*black arrow*). (**b**) A 15° blade is used to make a cut down perpendicular to Schlemm's canal. Once the canal has been entered, one can usually appreciate a "gush" of fluid or blood. The arrow is denoting the location of the canal. Sometimes, the canal is not where one would think it should be, especially in dysgenic angles. As such, one should make a large perpendicular cut down to ensure proper identification of the canal. (**c**) Once Schlemm's canal has been identified, a cut is made over the canal in a parallel fashion to allow for exposure to the canal and proper access with a suture or a micro-catheter. (**d**) The lighted micro-catheter is used to cannulate Schlemm's canal and ensure the catheter is in the correct location. (**e**) One can appreciate that the light is traveling along the circumference of Schlemm's canal. It has been passed nearly 90° at this point. (**f**) The lighted tip demonstrates the catheter has passed nearly 330°. One should be sure to watch the lighted tip as the catheter can occasionally go down a collector or in to the suprachoroidal space. (**g**) The distal catheter tip has been retrieved, after having passed 360° around the canal. (**h**) Applying traction on the proximal and distal ends of the catheter allows for creation of the trabeculotomy. The catheter can now be seen in the anterior chamber after having broken through the trabecular membrane. (**i**) A 360 circumferential trabeculotomy has been created with the catheter now externalized (*arrows*)



Surgical Approaches, Fig. 3 Gonioscopy-assisted transluminal trabeculotomy (GATT), trabeculotomy *ab interno*. (**a**) Initially, a goniotomy is created with a microvitreoretinal (MVR) blade. (**b**) Schlemm's canal is then cannulated with a micro-catheter, using microsurgical forceps. (**c**) One can appreciate that the catheter has already been passed 2–3 clock hours around Schlemm's canal. (**d**) Given the blinking red light on the distal end of the tip, one can follow the path of the catheter as it travels circumferentially around the canal. The catheter has passed 180° around the canal. (**e**) One can now appreciate that the micro-catheter has come full circle around the canal. (**f**) The distal tip of the catheter is retrieved within the anterior chamber using microsurgical forceps. (**g**) The distal tip of the catheter is then externalized through a paracentesis, and nearly 180° of the trabeculotomy has been completed. (**h**) Tension is placed on the proximal end of the catheter, thus completing the remaining 180° trabeculotomy. (**i**) A full circumferential trabeculotomy has been completed without violating the conjunctiva or sclera



Surgical Approaches, Fig. 4 Trabectome (**a**) Initially, the trabectome handpiece is inserted into the anterior chamber with the infusion in the "on" position. (**b**) The sharp tip of the probe is inserted through the trabecular meshwork. Care is taken to avoid damaging the back wall of Schlemm's canal. (**c**) Once treatment has been initiated, one can appreciate the white stripe representing the back wall of Schlemm's canal. Also note the bubbles near the leading tip of the probe. (**d**) Once treatment of the trabecular meshwork has completed, one is able to appreciate the trabecular groove and an open-angle drainage free of trabecular tissue. Anterior chamber aqueous now has direct access to the downstream collector system

Complications Common to Trabeculotomy

- A postoperative hyphema (most common).
  - Postoperative bleeding is most likely when the IOP drops below episcleral venous pressure (EVP). An intraoperative hyphema is usually a good prognostic indicator that the downstream collectors are intact. Observing an episcleral venous fluid wave is also a good sign.
  - To limit the amount of the postoperative hyphema, one can leave a 10–20% viscoelastic fill in the anterior chamber.
- An IOP spike (transient).
- Steroid-induced IOP elevation.
- A descemet's detachment or a hemorrhagic descemet's detachment can occur (rarely).

Outcomes

- Depending on the specific type of trabeculotomy performed, the success rates range anywhere from 50 to 90% (Grover et al. 2014).
- Developmental glaucomas and secondary open-angle glaucomas tend to do better than other advanced open-angle types of glaucoma.
- If the surgery goes without complication and the trabecular meshwork is removed as a source of resistance to outflow, then the IOP should fall into the mid to upper teens.
- Although direct comparisons between trabectome and circumferential trabeculotomy are not available, one can possibly conclude that treating more of the angle will result in better IOP lowering. This observation has been documented when comparing 360 circumferential filamentary trabeculotomy with segmental trabeculotomies created by a metal trabeculotome (Chin et al. 2012).

Keys to Success
- Understand angle anatomy from an internal and external perspective.
- Feel comfortable performing gonioscopy-assisted glaucoma surgery.
- A patient must have an intact inherent collector system in order for a trabeculotomy to be successful (therefore earlier disease likely will do better).

Procedure

Non-Penetrating Glaucoma Surgery (NPGS)

- **Canaloplasty** (Fig. 5)

Mechanism of Action

Circumferential viscodilation and tensioning of the inner wall of Schlemm's canal is believed to enhance flow into the natural collector channels.

Indications/Contraindications

Indications Open-angle glaucomas that are classified as mild to moderate. Eyes with moderate ocular surface disease where a bleb is not desirable are also candidates and works well in conjunction with cataract surgery.

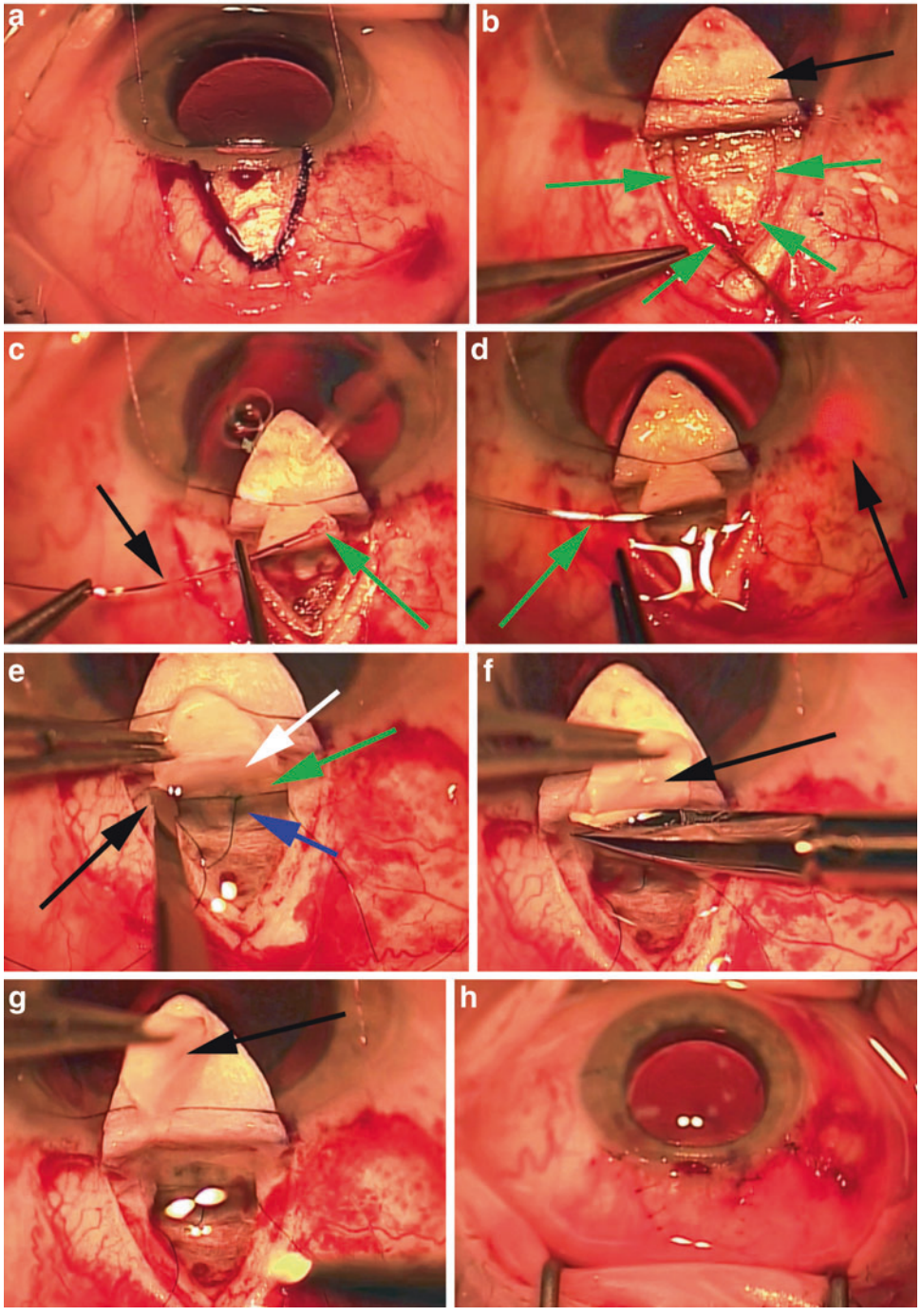
Contraindications Advanced glaucoma, closed-angle glaucoma, severe conjunctival scarring superiorly, uveitic glaucoma, and eyes that require a surgical peripheral iridectomy (PI) for PI is not carried out with canaloplasty.

Key Procedural Components
- Fornix-based conjunctival flap is easiest for complex limbal anatomic dissections.
- Create a superficial parabolic scleral flap (300–400 μm) followed by a second deep flap (600 μm) within the borders of the scleral bed.
- Some surgeons prefer to use mitomycin C to inhibit fibrosis at this stage.
- Unroof Schlemm's canal and fully visualize the canal.
- Some surgeons prefer to peel off the inner layer of Schlemm's canal, leaving the trabecular meshwork and trabeculodescemetic membrane (TDM).
- Viscodilate the cut ends of Schlemm's canal.
- Cannulate Schlemm's canal with a microcatheter (EllexiScience, Fremont, CA), and after 360°, tie on a 10-0 Prolene suture and retrieve iTrack for 360°. Inject viscoelastic every two clock hours during the retrieval. Trim and isolate the suture and tighten in the canal.
- Remove the deep flap, creating the deep sclerectomy, and secure the superficial flap.
- Close the conjunctiva in a watertight fashion.

Complications
- Postoperative hyphema common due to canal exposure
- Transient IOP elevation
- Anterior chamber perforation
- Descemet's detachment, rarely hemorrhagic
- Postoperative iris incarceration into TDM
- Hypotony possible but uncommon
- Dysesthetic bleb, not common
- Suture extrusion into anterior chamber

Outcomes
- A US-based prospective nonrandomized multicenter clinical trial demonstrated that at 3 years, all study eyes that underwent canaloplasty (n = 157) had a mean IOP of 15.2 mmHg 0±3.5 (standard deviation [SD]) and mean glaucoma medication use of 0.8 ± 0.9 compared to a baseline IOP of 23.8 ± 5.0 mmHg on 1.8 ± 0.9 medications (Lewis et al. 2011).
- A European-based prospective nonrandomized multicenter clinical trial demonstrated that at 3 years, all study eyes that underwent canaloplasty (n = 109) had a mean IOP of 15.1 ± 3.1 mmHg (SD) and mean glaucoma medication use of 0.9 ± 0.9 compared to a baseline IOP of 23.0 ± 4.3 mmHg on 1.9 ± 0.7 medications (Bull et al. 2011).

Keys to Success
- One must be able to construct two scleral flaps of adequate size and depth.



Surgical Approaches, Fig. 5 Canaloplasty (**a**) Outline of superficial scleral flap. The first flap is approximately 300–400 μm in thickness and fashioned into the clear cornea. (**b**) Formation of superficial flap and outline of deep flap. The *black arrow* designates the already fashioned superficial uniform flap, which is conveniently tacked down with the traction suture. The *green arrows* show the outline of the deep flap, which is all the way to the level of the suprachoroidal scleral fibers. (**c**) Completion of deep scleral flap and iTrack micro-catheter in position for canal entry. The *black arrow* delineates the illuminated flexible micro-catheter (200 μm), and the *green arrow*

- One must be able to create an ideal TDW and understand the required amount of tension that must be placed with the suture without breaking through the trabecular meshwork.

Procedure

iStent® (Fig. 6)

Mechanism of Action

A metallic microdevice that is aimed at bypassing the trabecular meshwork and creating a direct route from the anterior chamber to Schlemm's canal.

Indications/Contraindications

Indications Open-angle glaucomas that are classified as mild to moderate. In the US, this device must be placed in combination with cataract surgery and intraocular lens implantation.

Contraindications Advanced glaucoma, closed-angle glaucoma, uveitic glaucoma (relative), unmedicated IOP greater than 36 mmHg, and/or prior complicated glaucoma surgery.

Key Procedural Components

- Following an uncomplicated clear cornea cataract surgery, the same temporal wound is used.
- The stent on the tip of the injector is inserted through the clear corneal incision.
- The tip of the stent is inserted into Schlemm's canal with the aide of gonioscopy. The stent is inserted through the nasal trabecular meshwork and advanced slightly until the stent is secured into place and stable.
- Viscoelastic is removed, and wound management is similar to the conclusion of a typical cataract surgery.

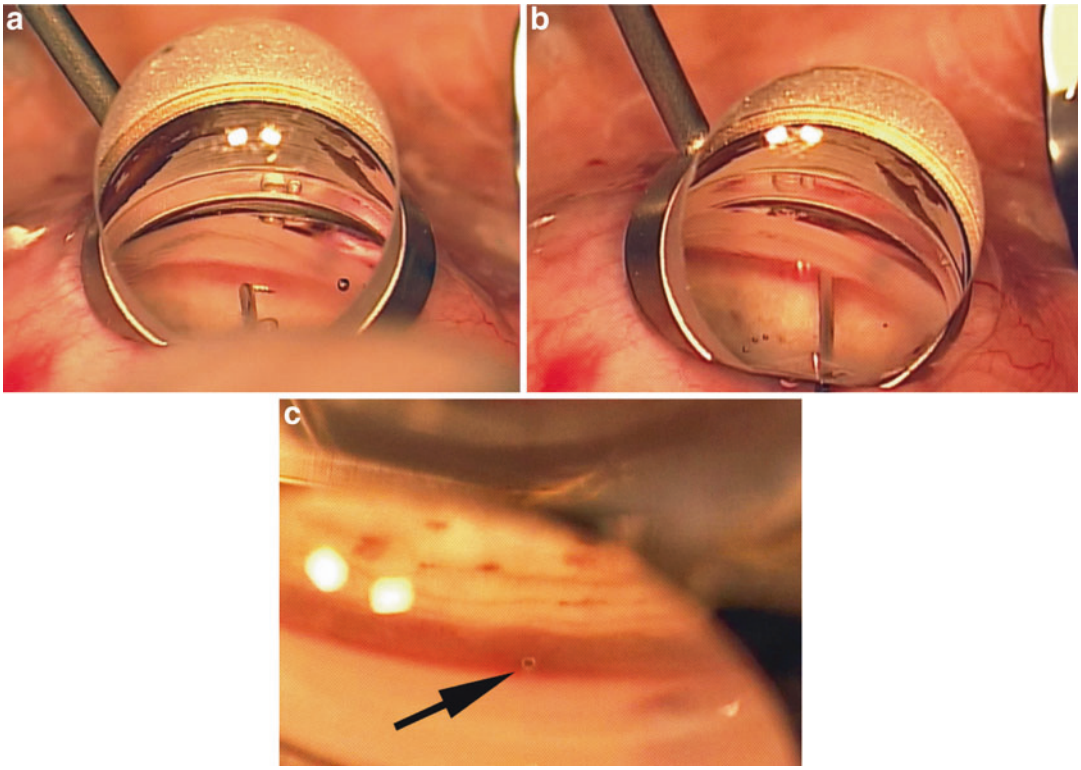
Complications

- Intraoperative
  - Iris touch of stent
  - Endothelial touch of stent
  - Stent malpositioning
- Postoperative
  - Inflammation
  - Stent malpositioning
  - Stent obstruction with the iris
  - IOP elevation
  - Hyphema

Outcomes

- A US-based prospective randomized controlled multicenter clinical trial demonstrated that at 2 years, the mean IOP in the stent group was 17.1 ± 2.9 mm Hg on a mean of 0.3 ± 0.6 medications. The mean IOP in the control group had increased to 17.8 ± 3.3 mm Hg on a mean of 0.5 ± 0.7 medications. At 24 months, the IOP in the stent group was 8.4 mmHg lower than the baseline medication washout IOP. In comparison, the IOP in the control group was

Surgical Approaches, Fig. 5 (continued) points to its tip, which is slightly larger in diameter (250 μm). (**d**) iTrack catheter in position in Schlemm's canal. The *black arrow* points to the illuminated tip of the iTrack, indicating its variable position in the canal. The illumination is very helpful to know the extent of canal traversed or if the device comes out of the canal. The proximal portion of the micro-catheter (*green arrow*) is kept in proper alignment to keep the catheter from coming out of the canal. (**e**) Suture in place in Schlemm's canal. With the suture in good position and tightened as necessary, the deep flap is further dissected (*black arrow*) to create the trabeculodescemetic membrane (TDM, *green arrow*). The TDM is the site of percolation of aqueous from the anterior chamber to the intrascleral lake which is created by removing the deep flap. As the deep flap is dissected, note the smooth area, *white arrow*, which is the roof of Schlemm's canal. The *blue arrow* is the floor of Schlemm's canal. (**f**) Deep sclerectomy. The deep flap (*black arrow*) is excised with Vannas scissors at its base. This is done in a very gentle fashion in order to avoid perforation into the anterior chamber. (**g**) Excised deep flap. The *black arrow* denotes the excised deep flap. The leftover space creates an intrascleral cavern for the enhanced egress of aqueous humor. (**h**). Closure of deep flap and conjunctiva. The superficial scleral flap and conjunctiva are closed in a watertight fashion. The authors close the flap to prevent any flow of aqueous that could form a bleb. Some surgeons close the flap so that a shallow bleb will form



Surgical Approaches, Fig. 6 iStent trabecular microbypass. (**a**) At the completion of phacoemulsification with PCIOL, the iStent inserter is visualized in the mid anterior chamber through a Swan-Jacob gonioprism. (**b**) The device is inserted into Schlemm's canal, slightly angled initially, then following the curve of the canal. The device is released once properly positioned in the canal. It takes considerable experience to complete this delicate maneuver. (**c**) Goniophotograph of properly positioned iStent

7.5 mm Hg lower than the baseline medication washout IOP (Craven et al. 2012).

Keys to Success

- One must be able to properly identify angle structure during intraoperative gonioscopy (specifically the scleral spur and trabecular meshwork).
- One must be comfortable with angle surgery.
- The stent must be confirmed, intraoperatively, to be in the correct place.

Incisional Glaucoma Surgeries that Create a New Artificial Drainage System

Procedure

Filtration Surgery (Fig. 7)

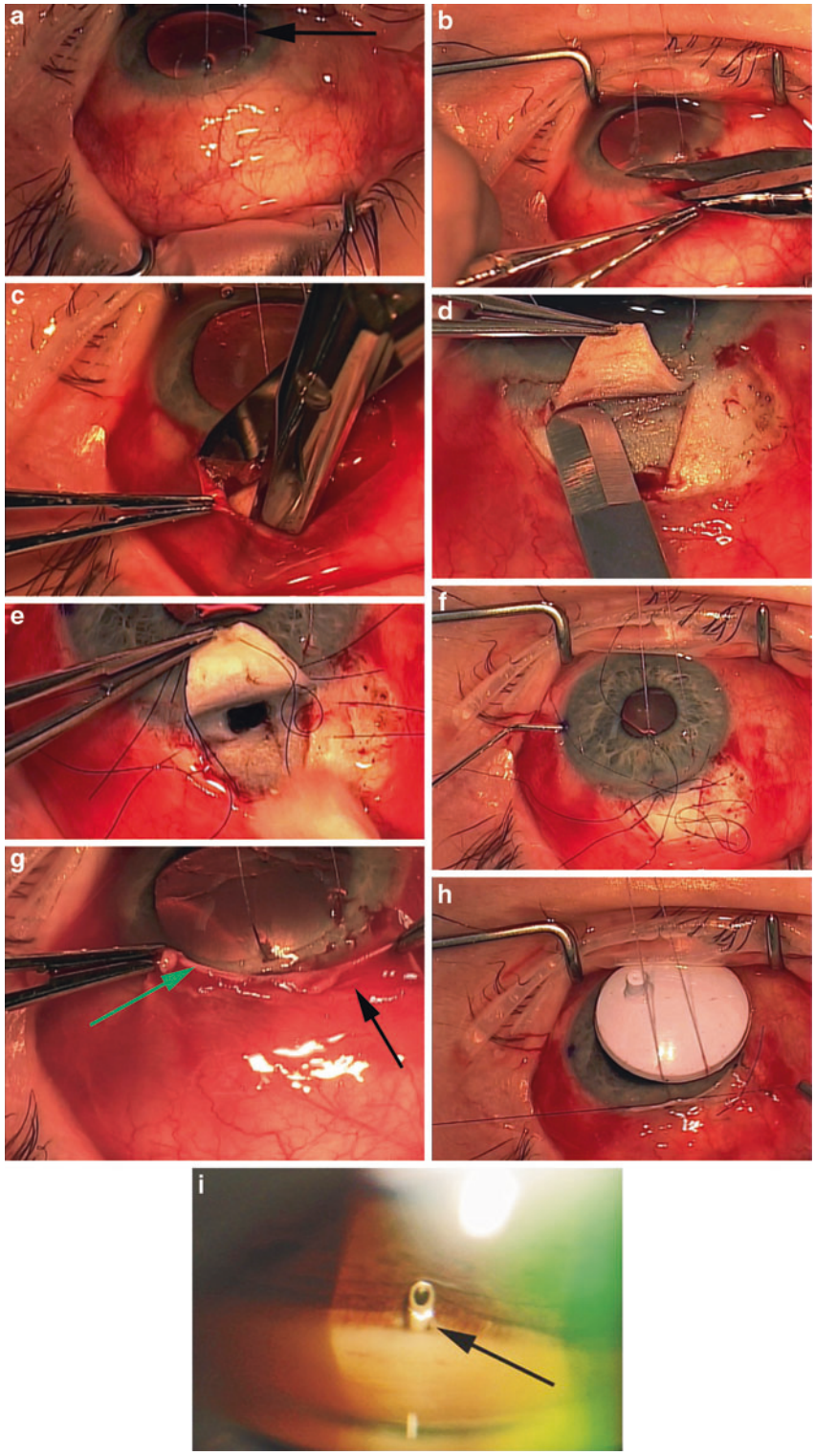
- Trabeculectomy
- EX-PRESS shunt

Mechanism of Action

Lowers IOP by diverting aqueous from the anterior chamber to the perilimbal subconjunctival region, producing a fluid-filled bleb cavity. Both procedures divert aqueous through the limbus, trabeculectomy by sclerectomy (removal of a block of tissue), and EX-PRESS through a miniature shunt.

Indications/Contraindications

Indications Most uncontrolled glaucomas, especially primary glaucomas (POAG, CACG), and combined phacotrabeculectomy for cataract glaucoma.



Surgical Approaches, Fig. 7 (continued)

Contraindications Severe conjunctival scarring; inflammation with altered blood aqueous barrier; limbal scleral scarring; moderate to advanced ocular surface disease such as rosacea, blepharitis, and pemphigoid; neovascular, inflammatory glaucoma; and epithelial downgrowth.

Key Procedural Components

- Decide on fornix versus limbal-based conjunctival flap. The authors prefer fornix-based approach.
- Obtain adequate exposure of the operative site.
- Fashion perilimbal flap, sclerostomy, and peripheral iridectomy.
- Closure of scleral and conjunctival flap.

Complications

- Choroidal effusion 14%
- Wound leak 12%
- Shallow or flat AC 10%
- Persistent corneal edema 9%
- Dysesthesia 8%
- Hyphema 8%
- Encapsulated bleb 6%
- Persistent diplopia 2%
- Hypotony maculopathy 5%
- Endophthalmitis/blebitis 5%

Outcomes

- TVT study (Gedde et al. 2012a): In the trabeculectomy arm of this study (4 mg/ml of Mitomycin C for 4 min in eyes with prior cataract or filtration surgery), 41 of 105 eyes failed due to uncontrolled IOP (17), reoperation for glaucoma (11), and persistent hypotony (13). At 5 years, IOP was 14.4 ± 6.9 mm Hg in the tube group and 12.6 ± 5.9 mm Hg in the trabeculectomy group, and the corresponding number of glaucoma medications was 1.4 ± 1.3 and 1.2 ± 1.5. The cumulative probability of failure was 29.8% in the tube group and 46.9% in the trabeculectomy group, and the rate of reoperation for glaucoma was higher in the trabeculectomy group.
- Hopkins review (Jampel et al. 2012): Target IOP was achieved at 4 years in 70% of eyes and was associated with progressive cataract and small risks of bleb-related complications. Approximately 14% of eyes had reoperation for glaucoma. Fornix-based procedures had a lower incidence of serious bleb-related problems.
- XVT study (Netland et al. 2013) EX-PRESS results: Mean intraocular pressure at 2 years after surgery was 14.7 ± 4.6 mm Hg and 14.6 ± 7.1 mm Hg in the EX-PRESS and trabeculectomy groups, with a respective success rate of 83 and 79% (MMC .25 mg/ml for 1–2 min for both groups). The vision was not significantly different compared with baseline at 1 month and after 3 months. The total number of postoperative complications was higher after trabeculectomy than after EX-PRESS implantation with a more rapid return to baseline vision in the EX-PRESS group.

Keys to Success

- Control inflammation before and immediately after surgery.
- Precise flap and sclerostomy construction with intraoperative flow through the scleral flap.
- Watertight closure of conjunctival flap to prevent wound leak.

S

Surgical Approaches, Fig. 7 Trabeculectomy. (**a**) The first surgical step is proper exposure of the operative site achieved with a corneal traction suture (*black arrow*). (**b**) A fornix-based conjunctival flap is useful for virgin eyes as well as eyes with prior conjunctival scarring. (**c**) Include Tenon's capsule in the dissection from the check ligaments at the limbus all the way posteriorly to create a sufficient subconjunctival space for a broad antimetabolite application. (**d**) Dissect a 2/3 thick uniform scleral flap to guard the sclerostomy. (**e**) A block of corneoscleral tissue is removed followed by peripheral iridectomy. (**f**) Titrate the flow through the scleral flap. (**g**) Inspect the edge of the conjunctiva (*black arrow*) and Tenon's capsule (*green arrow*) for closure and incorporate both into the limbal closure. (**h**) Close the conjunctiva and Tenon's capsule in a watertight fashion. (**i**) Goniophotograph of an EX-PRESS shunt used in place of making a sclerostomy

Procedure

Drainage Implant Surgery (Fig. 8)

- Baerveldt
- Ahmed
- Molteno

Mechanism of Action

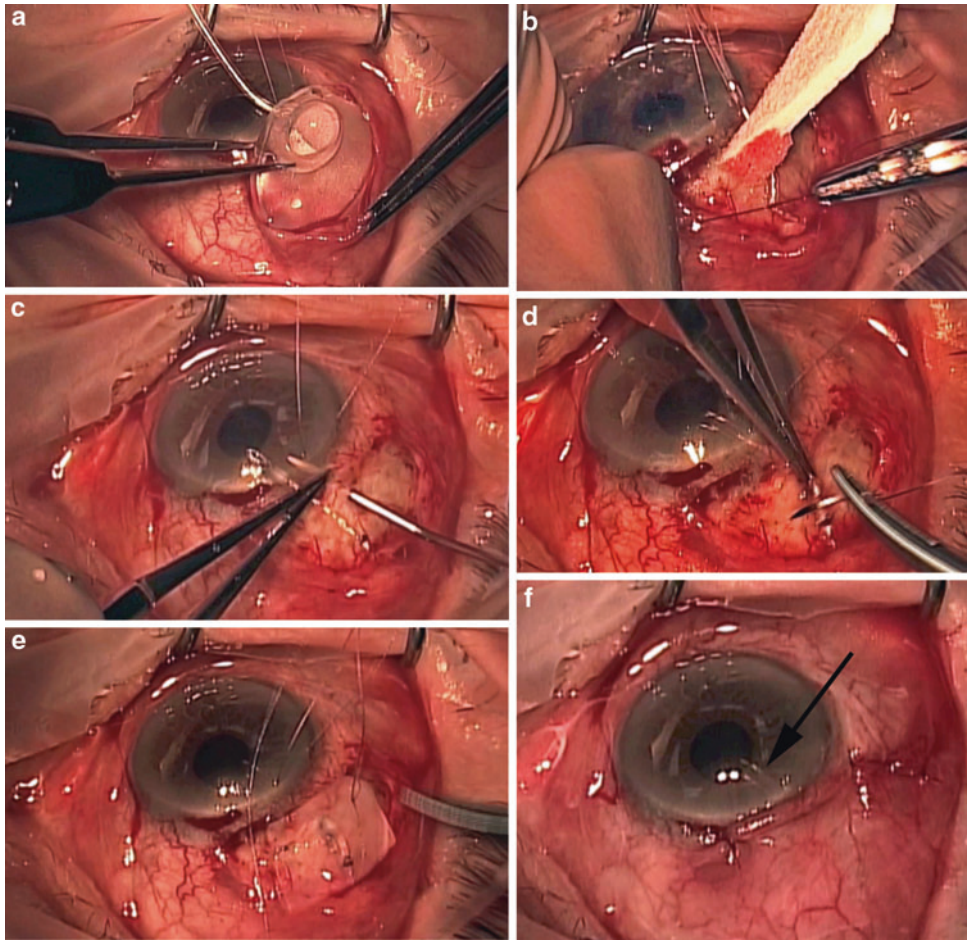
Lowers IOP by shunting aqueous from the anterior chamber to an equatorial bleb-promoting device

Indications

Uncontrolled primary or secondary glaucoma, phakic, aphakic, or pseudophakic. In high-risk eyes for hypotony or choroidal hemorrhage-related events, consider a two-stage approach or single-stage approach with controlled ligature release.

Contraindications

Insufficient conjunctiva to cover the device and difficulties in patients with encircling bands.



Surgical Approaches, Fig. 8 Glaucoma drainage implant surgery. (**a**) The device is inserted through a fornix-based incision and positioned and sutured to the sclera at the equator of the eye. (**b**) The tube is tied off with an 8–0 Vicryl absorbable suture in order to prevent immediate postoperative hypotony. The suture dissolves at 1 month and then aqueous flows to the plate. (**c**) A paracentesis is made with a 23-gauge needle in order to insert the trimmed tube. No viscoelastic is used at any time except for valved tubes such as an Ahmed. (**d**) The tube is vented with a needle to try and produce flow through the side of the tube in the immediate postoperative period. (**e**) A corneal patch graft is sutured over the tube to prevent erosion. (**f**) The conjunctiva is hooded over the device and secured to the limbus. The tube is easily seen in the anterior chamber (*black arrow*) in good position

Key Procedural Components
- Decide on fornix or limbal-based conjunctival approach.
- Decide on type of device, valved or non-valved.
- Affix device to equator of the sclera and place tube through a 23-gauge needle site.
- Ligate and vent the tube if non-valved.
- Cover the tube with corneal tissue.
- Complications.
- Persistent corneal edema 17%.
- Choroidal effusion 15%.
- Shallow or flat AC 11%.
- Persistent diplopia 6%.
- CME 5%.
- Tube erosion 5%.
- Tube obstruction 3%.
- Aqueous misdirection 3%.
- Suprachoroidal hemorrhage 2%.
- Endophthalmitis 1%.

Outcomes
- TVT study (Gedde et al. 2012b): The drainage implant arm of this study used the 350 sq. mm Baerveldt device. At 5 years, the cumulative probability of failure was 29.8%, 9% required further glaucoma surgery and 22% required reoperations for complications.
- AVB study (Christakis et al. 2013): At 3 years, the cumulative probability of failure was 51% in the Ahmed group and 34% in the Baerveldt group. Mean IOP was 15.7 ± 4.8 mmHg in the Ahmed group and 14.4 ± 5.1 mmHg in the Baerveldt group, and respective medications were 1.8 ± 1.4 and 1.1 ± 1.3. Postoperative interventions were 38% in the Ahmed and 50% in the Baerveldt. The Baerveldt group had a slightly higher rate of hypotony-related vision-threatening complications. Eleven percent of eyes required further glaucoma surgery. At 3 years, 25% of the Ahmed group and 50% of the Baerveldt group required no topical medications.
- ABC study (Budenz et al. 2011): At 1 year, postoperative IOP was 15.4 ± 5.5 in the AGV group and 13.2 ± 6.8 in the BGI group requiring 1.8 ± 1.3 and 1.5 ± 1.4 postoperative medications, respectively. Significant postoperative complications were noted in 20% of AGV and 34% in the BGI group, and cumulative probability of failure was 16.4% and 14%, respectively.

Keys to Success
- Adequately secure device to equator of the eye.
- Proper tube placement avoids iritis and corneal decompensation.
- Adequate coverage of tube with corneal tissue to prevent erosion.
- Adequate cover of tube and plate with conjunctiva may require extensive conjunctival dissection in some cases.

Procedure

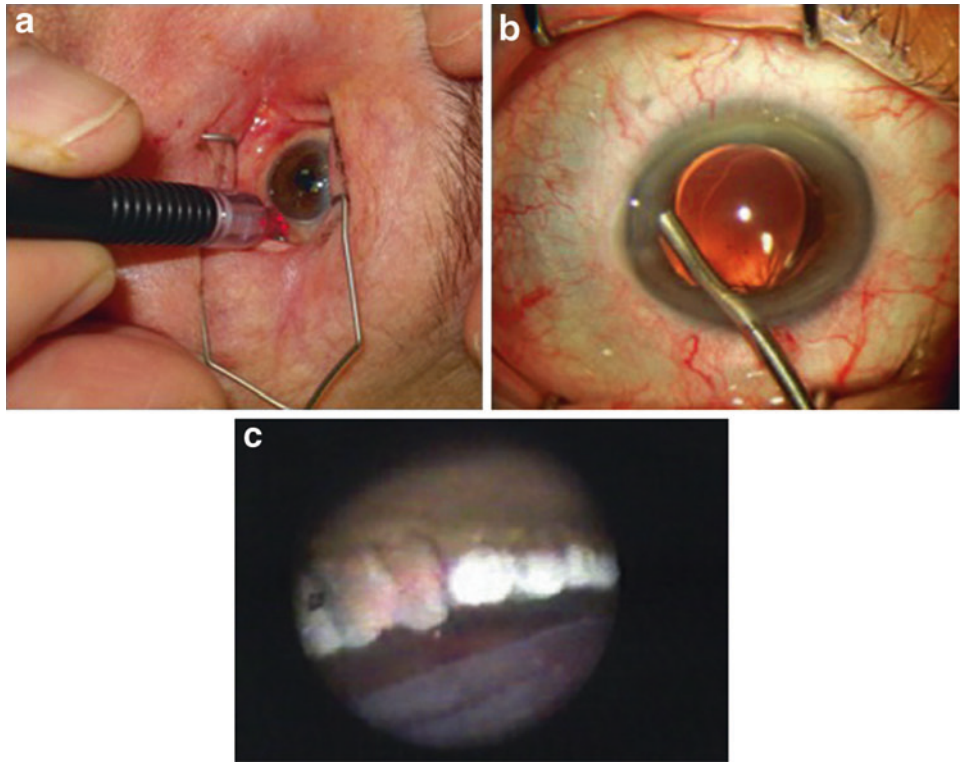
Cyclophotocoagulation (Fig. 9)

- Transscleral cyclophotocoagulation (TSCPC)
- Endocyclophotocoagulation (ECP)

Mechanism of Action
- A wavelength of 810 nm is used to directly laser the ciliary body processes (ECP) or indirectly through the sclera (TSCPC), and both methods lower IOP by reducing the formation of aqueous humor.

Indications
- Glaucoma and visually significant cataract.
- Plateau iris syndrome.
- Eyes with severe conjunctival scarring.
- High-risk eyes for choroidal events such as high myopia and bleeding tendencies.
- Aphakic or pseudophakic glaucoma.
- Refractory pediatric glaucoma.
- Uncontrolled glaucoma post-filtration surgery.
- TSCPC is an alternative for patients in poor health unable to tolerate intraocular surgery.

Contraindications
- Avoid ECP in phakic eyes due to lens damage.
- TSCPC may lead to long-term zonular damage in phakic eyes making future lens extraction more difficult.
- Pseudoexfoliation glaucoma.



Surgical Approaches, Fig. 9 Cyclophotocoagulation. (**a**) TSCPC. The G-probe (IRIDEX, Mountain View, CA) is applied to the limbus, directly over the ciliary body. Typically, 1200 mW for 4 sec duration is applied to three quadrants, sparing one of the quadrants in order to prevent hypotony. (**b**) The ECP 20-gauge microendoscope has a Xenon light source, 810 nm laser, and camera (Endo Optiks, Little Silver, NJ). (**c**) The ciliary body processes are visualized and targeted with the oval red aiming beam. The processes turn white and shrink the end point of the ablation

- Uncontrolled uveitis.
- Patients with altered anatomy preventing a view of the ciliary processes such as a Soemmering ring.

Key Procedural Components

- The most common use of ECP is to combine it with phacoemulsification; this is especially useful in narrow-angled eyes or eyes with plateau iris configuration.
- Upon completion of phacoemulsification, the anterior chamber is reformed with viscoelastic (Healon GV), making sure to elevate the iris away from the PCIOL.
- Insert the ECP probe through the cataract incision, visualize the ciliary body processes, and start the laser at .2 W. Increase the power until the ciliary body processes turn white and shrink.
- A second incision may be made for a 360° treatment.
- ECP requires approximately 200–400 mW of energy, while TSCPC energy settings are higher, at 1200 mW for 4 sec.

Complications

- IOP spike on day one
- Iritis (mild unless overtreated)
- Fibrin formation (rare)
- Cystoid macular edema (rare)

Outcomes

- ECP is effective after failed outflow procedures. In a prospective case series of 25 patients with uncontrolled IOP after drainage implant

surgery, IOP was reduced from 24–15 mm Hg, and medications were significantly reduced (Francis et al. 2011).
- A prospective study compared ECP to Ahmed implantation in refractory glaucomas post-failed filter and found a probability of success at 24 months of 70.59 and 73.5% for the Ahmed and ECP groups, respectively (Kima et al. 2004).
- Two-site phaco-ECP is more effective than one-site phaco-ECP with a mean IOP of 13 mm Hg versus 16 mm Hg without a higher incidence of complications (Kahook et al. 2007).
- A large retrospective study found TSCPC successful in 48% of eyes at a mean of 6 years (Lin et al. 2004).

Keys to Success
- Adequate treatment of ciliary processes, usually 360°.
- Avoid overtreatment which creates excessive inflammation.
- Avoid treating the posterior iris which leads to iritis.

Summary

The option to enhance flow through the patient's natural drainage system with canal-based or supraciliary surgery or rely on time-honored subconjunctival drainage with a filter or tube is now a critical preoperative question. As new surgical techniques evolve and preoperative assessment of the aqueous collector channels becomes available, surgeons will be able to predict the best possible procedure to serve their patient. When preoperative or intraoperative future testing reveals a collector system that appears salvageable, a canal-based procedure is reasonable. If the trabecular collector system appears atrophic, then potentially a supraciliary device may be useful. If the natural trabecular or uveoscleral channels are not salvageable, then either subconjunctival drainage with a filter or tube is necessary or potentially a procedure to reduce aqueous production. The key is the surgeon, and patients have the ability to tailor the surgery to the lifestyle and stage of disease. Patients with mild to moderate disease (with a presumably intact collector system), where an IOP in the mid- to high-teens is acceptable, may do well with a less-invasive canal-based surgery. The best place for a supraciliary device will likely be similar for canal-based procedures. Until our ability to assess the status of the trabecular and uveoscleral outflow system improves, patients with advanced disease who require lower IOP remain excellent candidates for more invasive filtration or tube-shunt surgery. Fortunately, outcomes with filtration surgery will continue to improve due to less-invasive filtration techniques as well as a better understanding of wound healing. The frequency of drainage implant surgery continues to rise as surgeons try to avoid limbal blebs and manage refractory glaucomas. However, complications from both filtration and tube surgeries are still problematic with blebitis, hypotony maculopathy, bleb failure, tube erosions, and double vision to name a few. Despite the numerous risks of trabeculectomy and glaucoma drainage implants, they are still the gold standard when a low IOP is critical to prevent further vision loss from glaucoma.

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Surgical Approaches to the Orbit

► Surgical Spaces, Orbital

Surgical PION

► Posterior Ischemic Optic Neuropathy

Surgical Spaces, Orbital

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Synonyms

Surgical approaches to the orbit

Definition

Surgical spaces, orbital

Structure

The bony orbit is comprised of seven bones (frontal, sphenoid, zygoma, maxilla, palantine, ethmoid, lacrimal) and may be roughly divided

into a lateral wall, medial wall, roof, and floor. Its anterior limit is the orbital septum. The boney orbit is configured in a cone shape with its apex posteriorly, and although it contains only roughly 30 cc of volume, it harbors an intricate network of nerves, vessels, and muscles all serving the function of the globe. Several fissures and foramina allow for the entrance and exit of nerves and vessels supplying the soft tissues of the orbit.

The orbital bones are lined with periosteum, also referred to as periorbita, which serves as a fibrous sling surrounding the orbital contents but also creates a potential space between the bone and periosteum. This *subperiosteal* space can sometimes harbor pathology (e.g., subperiosteal abscesses), but more frequently is utilized during surgical dissection.

The *extraocular muscles* constitute another surgical space. The four rectus muscles arise from the annulus of Zinn, which surrounds the opening of the optic canal. As the four rectus muscles travel anteriorly as the muscle cone, they become interconnected by an intermuscular septum; this anatomy is often referenced in surgical consideration of orbital lesions that are either "*intraconal*" or "*extraconal*." Notable structures in the extraconal space include the lacrimal gland and superior oblique.

Orbital fat fills and envelops any orbital space not occupied by other soft tissue structures and often obscures seemingly obvious (radiologically) lesions. Proximal to the globe itself, the fat is held back by Tenon's capsule, which fuses with the optic nerve sheath posteriorly. *Tenon's space* provides another point of surgical access to the orbit.

Finally, adjacent structures to the orbit may play a role in orbital pathology or surgical access and are referred to as the *extraorbital space*. These structures include the nose, sinuses, brain, skin, and conjunctiva.

Due to the complex nature of the orbit and the important functions it serves, a detailed understanding of orbital anatomy and its surgical spaces is required to safely operate within the tight confines of this boney cavity.

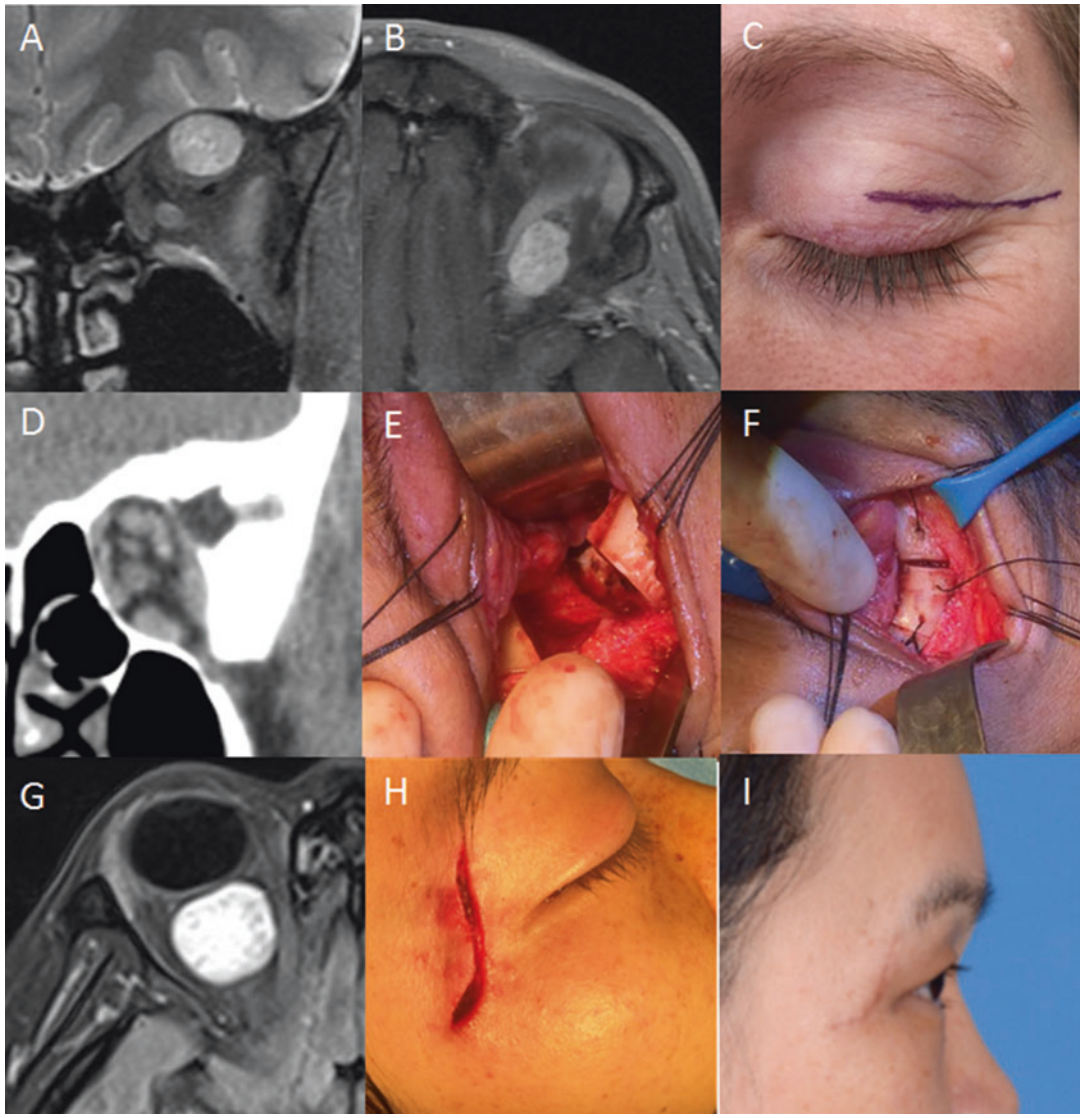
Clinical Relevance

When approaching the orbit surgically, one must consider many factors including the size, location, and nature of the lesion as well as the surrounding orbital anatomy and structures that would be encountered via each approach. In particular, one should note the position of the lesion relative to the optic nerve, so that the optic nerve will not be crossed during the approach. Surgical exposure and visualization are inherent challenges of operating within the deep, tight, confines of the orbit, and modification of those boney confines as described below may be considered depending on the size and location of the lesion. Surgical approaches can be roughly divided into lateral, medial, superior, and inferior approaches.

Lateral Approaches

To access lesions located laterally within the orbit, one often will utilize the natural crease of the upper eyelid as a point of access. This incision may be carried out laterally in an "extended lid crease" allowing for access to the lateral orbital rim and wall (Fig. 1a–c). The periosteum is incised along the lateral rim and a subperiosteal dissection carried out posteriorly where the zygomaticotemporal and zygomaticofacial neurovascular bundles may be encountered and often sacrificed. The periosteum may then be incised over the approximate depth of the lesion, and blunt dissection is carried out until the lesion is identified. Tagging the lateral, superior, or medial rectus anteriorly prior to surgery may facilitate identification of these muscles more posteriorly, either for direct biopsy or simply for orientation purposes. These muscles may then be retracted to provide further access to the intraconal space. This approach may be used to access the subperiosteal, extraconal, or intraconal spaces.

A similar surgical space may be accessed via simple lateral canthotomy and cantholysis followed by subperiosteal dissection posteriorly. While this provides reasonably good access to the lateral wall, it is somewhat more limited than the extended lid crease incision and therefore is



Surgical Spaces, Orbital, Fig. 1 Lateral approaches to the orbit: extended lid crease (without bone flap) to access a recurrent schwannoma (**a**–**c**), extended lid crease with bone flap used to approach posterior boney tunnel of orbital dermoid (**d**–**f**), and Kronlein approach with bone flap used to approach large cavernous hemangioma (**g**–**i**)

reserved for smaller or more anteriorly located lateral orbital lesions.

Conversely, particularly large lesions or lesions located more posteriorly in the lateral orbit may require more exposure, visualization, and space than a simple extended lid crease incision can provide. In these instances, a lateral bone flap should be considered. The approach is the same as an extended lid crease, except that prior to opening the periosteum, a segment of the lateral wall usually extends from the frontozygomatic suture line superiorly to the inferior curvature of the zygoma inferiorly and broken off at the zygomaticosphenoid suture line posteriorly (Fig. 1d–f).

Historically, this lateral orbitotomy with bone flap was performed with a Kronlein approach. This approach is similar to that of an extended lid crease, except the point of access is a "lazy S"-shaped incision directly over the lateral

rim and extending from the lateral brow to the zygoma (Fig. 1g–i). While providing excellent access, most have now come to adopt the extended lid crease incision as its incision is more cosmetically hidden without compromising exposure.

Lateral bone flaps may also be used in conjunction with other approaches for the sole purposes of providing additional space to improve visibility.

Medial Approaches

Accessing medially located lesions can sometimes be more challenging due to anatomic constraints; the location of the nose makes the medial orbit more confined via anterior approaches, and several medially based structures must be considered during dissection, including the ethmoidal arteries and supraorbital and supratrochlear neurovascular bundles.

One long-standing approach to the orbit is a Lynch or modified Lynch incision, which is a curvilinear incision in the shadow at the base of the bridge of the nose. It provides direct access to the periosteum, which can be incised and elevated laterally to expose the medial subperiosteal space. This incision remains a valuable approach to the orbit when the subperiosteal space is targeted (e.g., subperiosteal abscesses) and/or when a cutaneous drain is going to be left postoperatively.

However, there are several more cosmetically pleasing alternatives to the Lynch incision, which should be considered first. Much like the lateral extended lid crease incision, the medial lid crease can also be utilized as a well-guised access point to the medial orbit. The septum can either be directly incised or followed superiorly to the periosteum to access the subperiosteal space. Care must be taken around the trochlea and supratrochlear and supraorbital neurovascular bundles. A medial lid crease incision is commonly used for optic nerve sheath fenestrations, but may be used for any superomedial orbital lesion in the anterior half of the orbit (Fig. 2a).

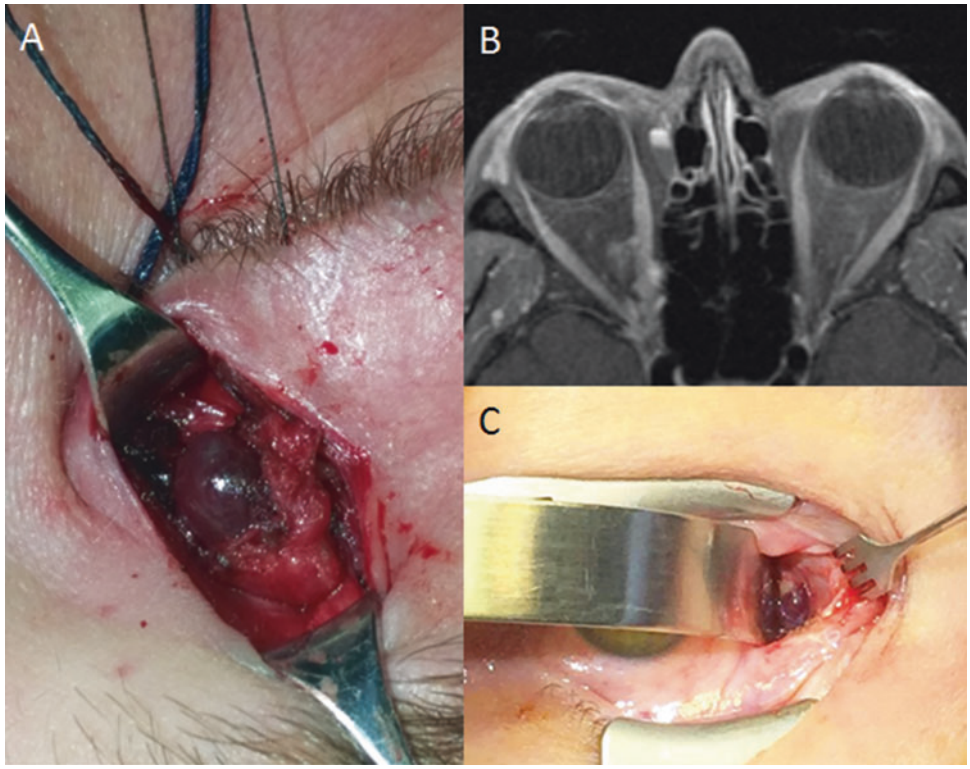
Most recently the transcaruncular approach was described and has become a popular approach to the medial orbit as it provides excellent access with a nearly imperceptible conjunctival incision between the caruncle and plica semilunaris. Dissection is carried medially in this space to reach the posterior lacrimal crest, which is subsequently incised, and the periosteum elevated posteriorly. Despite the minimal incision, this approach provides a surprising degree of access and exposure to the medial orbital space (Fig. 2b, c). Much like the Lynch incision (or lateral orbitotomy approaches described above), this incision commences its approach to the orbital contents from the subperiosteal space and therefore is particularly well suited for extraconal lesions.

For medially based, intraconal lesions, one may want to consider instead a transconjunctival approach in which a limbal incision with relaxing incisions is made and blunt dissection carried posteriorly in the sub-Tenon's space along the globe. The advantage of this approach is its direct access to the intraconal space, but it does have somewhat more limited exposure than a transcaruncular incision. This approach can also be used to access the optic nerve sheath for fenestration in conjunction with disinsertion of the medial rectus muscle. If the exposure for a particular lesion is too constricted by the eyelid, a lid-splitting procedure can also be performed with the transconjunctival approach. While this heals well and can provide ample exposure, some patients may still be cosmetically adverse to lid-splitting procedures.

Finally, while the extraorbital spaces such as the nose and sinus may be anatomic nuisances to the external medial orbital approaches, in some instances they provide excellent access to the medial orbital wall and floor. This is perhaps most frequently utilized in medial wall decompressions. However, some medially oriented tumors can and are removed via endoscopic approach. Endoscopic decompression of the medial orbit can also be utilized in concert with a lateral orbitotomy to create additional space when resecting particularly large or posterior orbital lesions.

Superior Approaches

For superiorly based lesions, lid crease or transconjunctival approaches as described above often provide sufficient access with maximal cosmesis



Surgical Spaces, Orbital, Fig. 2 Approaches to the medial orbit: medial lid crease approach to embolized varix (**a**) and transcaruncular approach to anterior tip of lymphatic malformation (**b** and **c**)

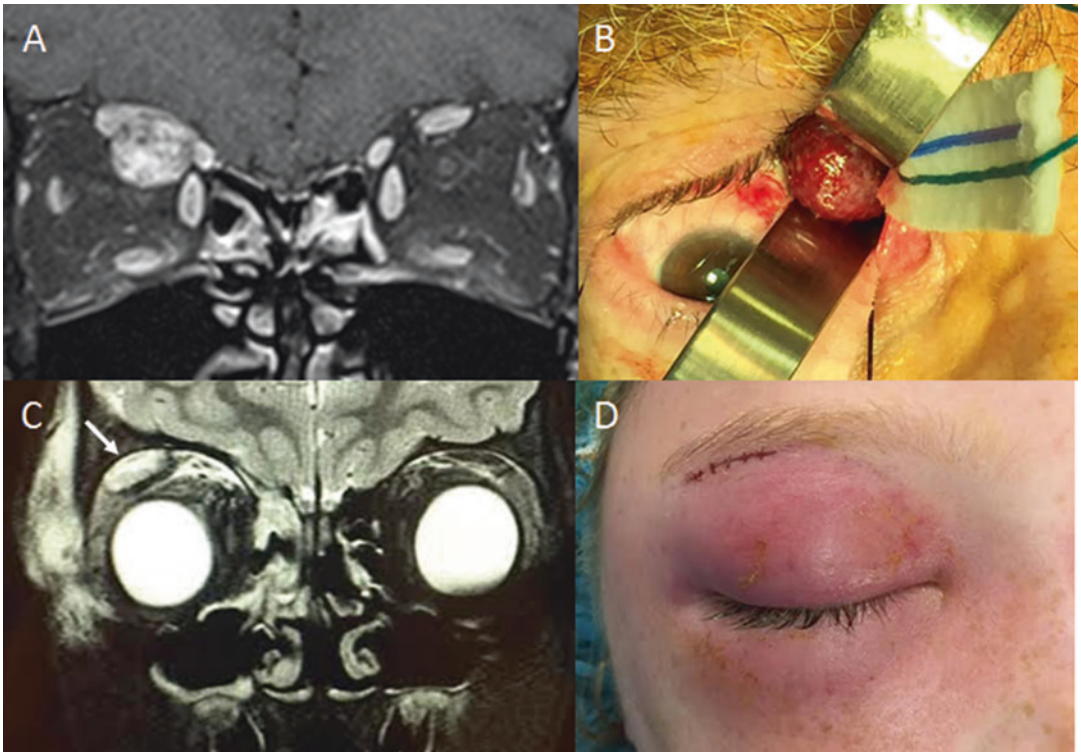
(Fig. 3a, b). However, a direct sub-brow incision may be considered and preferable in certain instances such as large dermoid cysts, frontal sinus mucoceles (not amenable to endoscopic treatment), and superiorly based subperiosteal abscesses (Fig. 3c, d). Much like the Lynch incision medially and the Kronlein incision laterally, this provides easy and direct access to the subperiosteal space, but is less cosmetically appealing and therefore is utilized in more limited instances.

While the majority of the superior orbit may be approached anteriorly, very posterior (i.e., apical) lesions or lesions with concomitant intracranial pathology may need to be approached transcranially (see section "Approaches to the Apex" below).

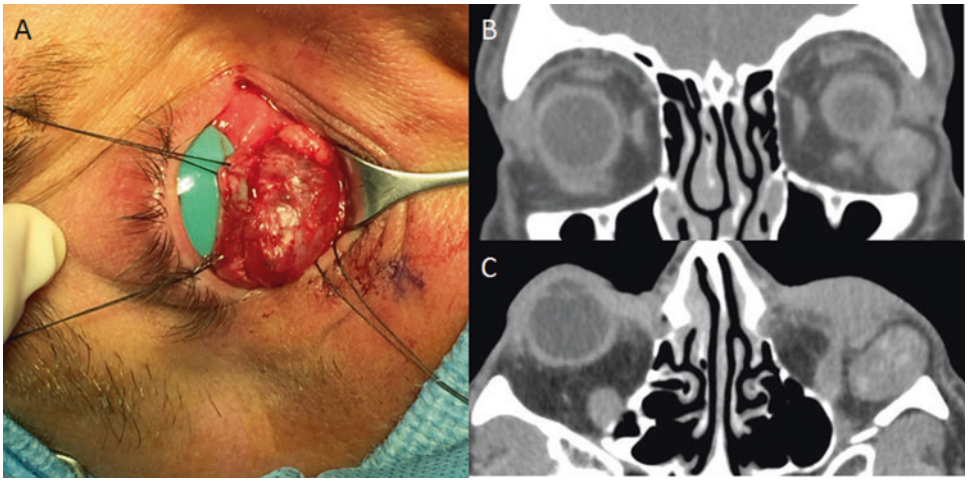
Inferior Approaches

Transconjunctival approaches to the orbit are frequently used due to their innocuous incision and ample access to the orbital floor. It may be combined with a lateral canthotomy and cantholysis ("swinging eyelid procedure") in eyelids with minimal laxity so as to avoid iatrogenic marginal tears during retraction. After a transconjunctival incision is made well below the level of the tarsus in the inferior fornix, a preseptal plane is bluntly followed to the inferior orbital rim where the periosteum is incised and elevated superiorly. This approach is used most frequently in orbital floor fracture repair, but can also be used for inferior rectus muscle biopsies or any inferiorly located tumors (Fig. 4a).

A subciliary approach may also be used by a similar dissection along a preseptal plane to the inferior orbital rim (Fig. 4b, c), though this approach is used less frequently primarily due to the excellent exposure that can be achieved with a more concealed transconjunctival approach, but also in part due to the risk of postoperative lower eyelid retraction.



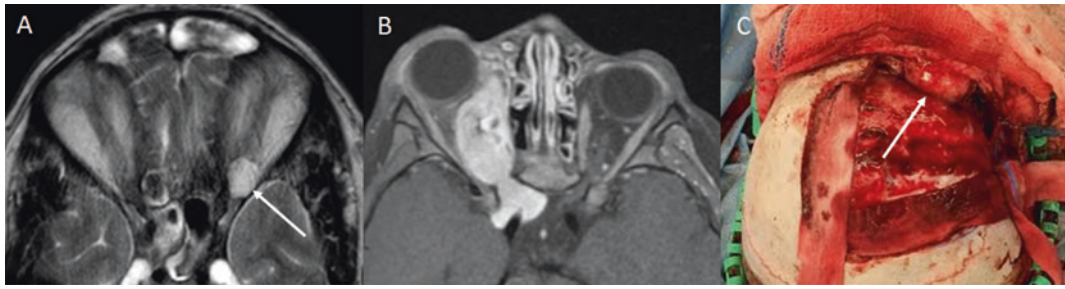
Surgical Spaces, Orbital, Fig. 3 Superior approaches to the orbit: transconjunctival approach to superomedial cavernous hemangioma (**a** and **b**) and a superior subperiosteal abscess (*arrow*) drained via a subrow incision (**c**–**d**)



Surgical Spaces, Orbital, Fig. 4 Inferior approaches: transconjunctival incision to access cystic inferior orbital mass (**a**) and clinical example of inferior orbital lesion (cavernous hemangioma) accessed via a subciliary incision (**b** and **c**)

Approaches to the Apex

As one travels more posteriorly within the orbit, the space becomes increasingly confined and difficult to visualize. Much as the boney walls converge, so too do the cranial nerves, muscles, and arteries. Thus, apically located lesions are



Surgical Spaces, Orbital, Fig. 5 Approaches to the apex: clinical example of apical cavernous hemangioma (*arrow*) approached transcranially (**a**), transcranial approach to an optic nerve glioma extending beyond the optic nerve canal (**b** and **c**, with *arrow* pointing to superior orbital contents)

both more difficult to access and more dangerous to remove. This constellation of difficulty often precludes an anterior approach.

In these instances, transcranial access is frequently the preferred approach. A craniotomy carries increased surgical risk independent of those risks associated with orbital surgery, and therefore the surgical threshold for apical lesions that cannot be approached anteriorly is higher. Nevertheless, when required, transcranial approaches can provide superb exposure to the orbital roof and apex, thereby providing the best chance for a safe orbital dissection (Fig. 5).

A particularly challenging orbital location to access is the inferior apex. As mentioned previously, one should make every attempt to craft a surgical approach that does not require crossing the path of the optic nerve. In these instances of posterior lesions located inferior to the optic nerve, endoscopic approaches may provide a safer alternative, though at the expense of exposure and direct visualization.

Cross-References

- ▶ Sinuses
- ▶ Sphenoid Bone
- ▶ Superior Orbital Fissure
- ▶ Zygomatic Bone
- ▶ Zygomaticofacial Canal
- ▶ Zygomaticotemporal Canal

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Surgically Induced Astigmatism

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Synonyms

SIA

Definition

Any change (increase or decrease) in astigmatism (subjective or objective, direction or magnitude, as indicated by vector analysis, e.g., as described

by Alpins (2001)) caused by a surgical intervention is called surgical induced astigmatism (SIA). In the majority of cases, however, the phrase refers to a change in corneal astigmatism caused by the incision in cataract surgery, refractive lens exchange (RLE), or phakic intraocular lens (PIOL) implantation. Nevertheless, the correction of astigmatism in excimer laser surgery or the reducing of astigmatism in keratoconus patients using intracorneal ring segments use, among many others, of course also SIA.

Epidemiology

Not applicable.

History

Focusing on the change of astigmatism due to the incision in cataract surgery, RLE, or PIOL implantation, different authors have provided data. The very first systematic description of SIA refers to refractive surgery. *Lans* in Leiden showed the effect of corneal incisions to correct corneal astigmatism in 1896, *Sato* in Tokyo followed in 1939. This procedure was later extensively used and modified by *Fjodorov*, beginning in the 1970s, to correct ametropia (RK – refractive keratotomy). Due to sub-prime visual results, regression, and severe adverse events, RK today is an obsolete procedure. Nevertheless, the development of corneal relaxing incisions to correct astigmatism went on, and today these methods are still in use in refractive and especially in cataract surgery (LRI, AK). Recently, many authors evaluated the SIA in cataract surgery and PIOL implantation. Either as regular astigmatism (Kohnen and Klaproth 2009, 2011) or referring also to higher order aberrations (which can be seen as irregular astigmatism) (Bühren et al. 2004).

Clinical Features

Corneal, limbal, or scleral incision in cataract surgery, refractive lens exchange, or PIOL implantation cause a change in corneal astigmatism. The magnitude of this change is determined by the size and location of the incision. The more central the incision is placed, the more SIA is caused. Further on temporal incisions cause less astigmatism and show better predictability than nasal or superior incision. Temporal clear-cornea incisions of 2.5 mm or less cause almost no significant change in corneal astigmatism. Astigmatism neutral incisions allow the surgeon to plan surgery without using nomogrames for SIA, which increases the predictability of the refractive outcome (Kohnen and Klaproth 2009, 2011). Today the problem of irregular SIA arises for any type of surgery that requires primary only one clear-cornea, limbal, or scleral incision larger than 2.5. Example for nonfoldable PIOL implantation is determined by the smallest implant diameter, which is usually the optics diameter. Such incisions of, e.g., 6 mm lengths cause significant (irregular) SIA at the site of the incision (Bühren et al. 2004) (Fig. 1).

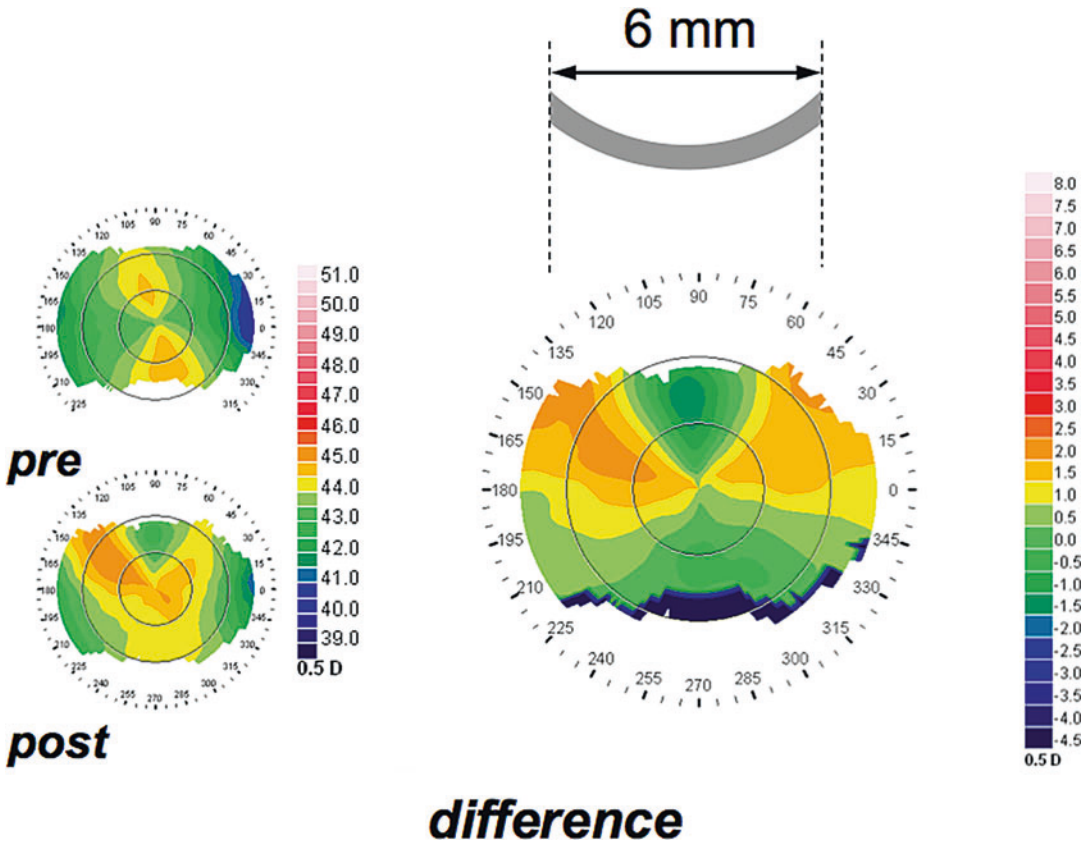
When planning implantation of such lenses, the SIA has to be taken into account preoperatively.

Tests

To quantify SIA pre- and postoperative assessment of astigmatism is required. This can either be performed subjectively by means of manifest refraction or by objective methods, such as keratometry or, more precise, Placido and/or Scheimpflug topography.

Treatment

The treatment of choice for surgical induced astigmatism is (a) to avoid it by performing surgery with microincisional surgery (<2.5 mm) or (b) to use its occurrence in a controlled manner to correct preexisting corneal astigmatism. Such options are the positioning of the incision on the steep meridian, the enlargement of the incision, opposite clear corneal incisions (OCCI), and limbal relaxing incisions (LRI). Different nomograms have been published on this topic; Table 1 shows an example by Wang et al. (2003).



Surgically Induced Astigmatism, Fig. 1 Topography of surgical induced astigmatism caused by implantation of a nonfoldable phakic intraocular lens through a 6 mm superior limbal incision. *Top left*: Preoperative topography. *Bottom left*: Postoperative topography. *Right*: The difference map represents the surgical induced astigmatism

Surgically Induced Astigmatism, Table 1 Nomogram for planning limbal relaxing incisions combined with cataract surgery by Wang et al. (2003)

Preoperative astigmatism (D)	Age (years)	Number of incisions	Lengths of incisions
0.75–1	<65	1	45°
	>65	2	45°
1.01–1.75	<65	2	60°
	>65	2	45°
≥1.76	<65	2	80°
	>65	2	60°

Cross-References

- ▶ Accommodation, Cataract
- ▶ Astigmatic Keratotomy
- ▶ Astigmatism
- ▶ Cataract Surgery
- ▶ Clear Corneal Incision
- ▶ Limbal Relaxing Incisions

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Surreptitious Illness

▶ Munchausen Syndrome

Suspicious Pigmented Choroidal Lesions

▶ Indeterminate Melanocytic Lesions of the Choroid

Sutureless Scleral Fixation

▶ Scleral Tunnel

Sutures (Surgical), Quickert, for Involutional Entropion

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Synonyms

Everting sutures

Definition

Quickert sutures are double-armed full-thickness sutures placed within the eyelids that exert an everting force upon the eyelid and were first described by Quickert and Rathburn in 1971 (Quickert and Rathbun 1971).

Indication

Quickert sutures are indicated in the surgical management of acute eyelid entropion, mild or intermittent involutional entropion, and congenital epiblepharon. Due to its simplicity and its suitability as an office procedure, Quickert sutures are often used as a temporizing method to achieve eyelid eversion prior to more permanent procedures in involutional entropion. In spastic entropion, the easy reversibility of the procedure allows for effective and temporary correction of acute entropion.

Quickert sutures may also be combined with more invasive procedures that surgically correct eyelid entropion in the operating room. Quickert sutures advance lower eyelid retractors, result in anterior rotation of the eyelid margin, and counteract overriding of the preseptal orbicularis by inducing fibrotic adhesion between the orbicularis and the lower eyelid retractors (Quickert and Rathbun 1971; Barnes et al. 2006). Quickert sutures do not address horizontal eyelid laxity and as a result have been noted to be especially effective in combination with procedures that reduce horizontal laxity such as the tarsal strip procedure (lateral tarsal strip) (Barnes et al. 2006).

Contraindication

Quickert sutures are contraindicated in eyelid ectropion. Quickert sutures are simple, minimally invasive, and easily reversible and are thus considered to be a relatively low-risk procedure. With exception to situations where there is greater operative risk to the patient, Quickert sutures are not commonly performed in isolation when more permanent correction of entropion is desired, due to long-term recurrence associated with the procedure.

Techniques and Principles

The Quickert procedure, as described by Quickert and Rathburn in the 1971 Archives of Ophthalmology manuscript, is as follows:

1. After skin preparation, infiltrate locally administered anesthetic agent subcutaneously and subconjunctivally along the inferior border of the tarsus.
2. Pass one needle of a double-armed 4-0, 5-0, or 6-0 suture adjacent to the inferior border of the tarsus from the conjunctival side, bringing it out through the skin in the same horizontal plane while pulling the skin inferiorly with light traction while the needle penetrates the orbicularis muscle and skin.
3. Pass the second arm of the suture similarly through the fornix 3 mm from the first needle, on the same horizontal plane.
4. Complete the suture over skin using the two ends of the double-armed suture. The knot should be tied as tight as possible without a bolster.
5. Repeat steps 2–4 and place a total of two to three sutures within the lateral aspect of the eyelid.

Outcome

The Quickert procedure is a relatively safe, low-risk procedure that is particularly useful in the management of acute entropion. However, it has been associated with long-term recurrence of entropion when used alone. When long-term correction of entropion is desired, other more invasive surgical procedures such as the Wies procedure, Jones procedure, and lateral tarsal strip procedure have traditionally been preferred. These procedures lack the simplicity of the Quickert procedure and are generally performed in the operating room, but have been shown to have a lower rate of long-term recurrence.

Often, the Quickert procedure provides a temporary option in the management of complications associated with eyelid entropion in the acute setting, such as keratopathy, prior to more invasive surgical correction. Furthermore, there have been numerous reports describing the use of the Quickert procedure in combination with the other surgical methods of entropion correction. The Quickert procedure has been described in combination with the lateral tarsal strip procedure (Barnes et al. 2006) and has been shown to be a procedure that was effective yet simple enough for use by a comprehensive ophthalmologist. A prospective randomized controlled trial that evaluated Quickert sutures alone versus lateral tarsal strip with everting sutures noted that Quickert sutures alone were associated with more long-term recurrence, consistent with findings noted from prior studies.

Complications

By nature of its simplicity and low-risk profile, serious complications associated with the Quickert procedure are uncommon. However, as with any surgical procedure, there is the risk of failure of achieving the intended purpose of surgery, or adequate correction of entropion with the Quickert procedure. Long-term recurrence, overcorrection with secondary ectropion, bleeding, infection, and injury to surrounding structures are other complications that may be associated with the procedure. With the eye within close proximity, exceptional care should be utilized to prevent injury to the globe, especially when the procedure is performed under local anesthesia without muscular paralysis that would reduce the risk of unexpected movements from the patient. The use of a suture confers a risk of granuloma formation, cheese wiring, and risk of wound dehiscence.

Cross-References

- ▶ Congenital Entropion
- ▶ Tarsal Strip Procedure
- ▶ Wies Repair

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Sweat Glands of Eyelid

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Definition

The sweat glands of the eyelid are eccrine or apocrine, located close to the eyelid skin surface and can give rise to various eyelid pathologies.

Structure

The skin of the eyelid is thinner than other parts of the body and contains both sweat glands and hair. Eccrine glands are the most common sweat gland on the body and consist of a single duct with a deeper coiled component, known as the glomerulum. The apocrine sweat glands, on the contrary, are located mostly in the axilla, nipple, external ear, external genitalia, and eyelids. The apocrine glands are larger than eccrine glands and are more numerous in the lower eyelid, and their ductal openings are closely associated with eyelashes. The eyelid also contains glands of Moll, which are modified apocrine sweat glands found at the margin of the eyelid, next to the base of the eyelashes and anterior to the meibomian glands.

Function

As in other parts of the body, the primary function of eccrine sweat glands on the eyelid is thermoregulation by secreting sweat. The eccrine glands also produce secretions to create a slightly acidic film on the surface of the skin that serves as a barrier to harmful microbial colonization. The apocrine glands largely begin to function during puberty and produce a secretion that is thicker than eccrine glands, which provides nutrients for healthy bacteria on the skin surface. The exact function of glands of Moll is unknown; however, these glands contain bacteriolytic enzyme lysozyme, membrane-associated mucin 1, immunoglobulin A, and its secretory component, which suggests a function in local immune defense (Stoeckelhuber et al. 2003).

Clinical Relevance

The sweat glands of the eyelid can give rise to various pathologies. Syringomas are benign lesions of the eyelid sweat glands, which are more common in women and classically present as crops of small, firm, skin colored papules (Ciarloni et al. 2016). A hydrocystoma is a translucent cyst located near the lid margin, usually resulting from blockage of the sweat glands of the eyelid.

There are a number of tumors and cysts that are derived from the eyelid sweat glands (Baker et al. 2016). The pathology of the tumors is varied and includes mucinous carcinoma, microcystic adnexal carcinoma, endocrine mucin-producing sweat gland carcinoma, eccrine carcinoma, apocrine carcinoma, poorly differential adnexal carcinoma, and hidradenocarcinoma. Most of these lesions can be managed using Mohs micrographic excision with excellent outcomes.

Cross-References

▶ Glands of Krause, Glands of Moll, Glands of Wolfring, Glands of Zeis
▶ Meibomian Glands

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Sweat Glands of Eyelid, Tumors Arising in

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Synonyms

Apocrine cystadenoma; Apocrine retention cyst; Black hidrocystoma; Moll's cyst; Sudoriferous cyst; Tumors of apocrine origin; Tumors of eccrine origin

Definition

Apocrine glands in the eyelids or the glands of Moll are located near the eyelid margin. They are composed of a secretory coil, an intradermal duct, and an intraepithelial duct. The secretory cells project their cytoplasm into a coiled lumen, which releases these secretions into the ducts, a process called decapitation secretion. Apocrine glands respond to sympathetic adrenergic stimuli and first become functional at puberty via hormonal stimulation. The primary function of eccrine glands is thermoregulation, through the cooling effects of evaporation of sweat on the skin's surface (Shields and Shields 1999; Albert and Jakobiec 2008).

Characteristics

Apocrine hidrocystoma is a very common smooth cyst from the gland of Moll. It is freely mobile and translucent and transilluminates light. It has been reported to be associated with ectodermal dysplasia. Treatments involve marsupialization for smaller lesions and complete excision for deeper lesions.

Cylindroma is a benign apocrine sweat gland lesion. It is dome-shaped, skin-colored nodule that occurs on the face and scalp. Multiple cylindromas can be autosomal dominantly inherited and can cover the entire scalp, known as a turban tumor. Treatment involves surgical excision.

Adenocarcinoma of the gland of Moll is an extremely rare apocrine sweat gland carcinoma. Many presumed cases have been confirmed to be sebaceous carcinoma and the pathology in reported cases has been disputed.

Eccrine hidrocystoma is a common translucent cystic lesion that clusters around the lower eyelids. They are considered ductal retention cysts and enlarge with perspiration, heat, and humidity. Treatment involves surgical excision.

Syringomas are benign eccrine tumors commonly found on young females. They are characterized as bilateral, small, waxy, pale yellowish nodules on the lower eyelids or upper cheeks. They tend to occur during puberty and are also found also in the axilla and sternal regions. Treatment involves surgical excision.

Eccrine spiradenoma is an uncommon benign lesion that presents as a deeper nodule beneath normal skin, which may be tender and painful. It tends to occur in early adulthood. Treatment is surgical excision.

Eccrine acrospiroma or clear cell hidradenoma is a rare, solid or cystic, mobile, skin- to red-colored nodule, just beneath the skin. Treatment is surgical excision.

Primary mucinous carcinoma or adenocystic carcinoma is an eccrine sweat gland carcinoma. It may present as a firm, flesh-colored nodule that transilluminates light; however, findings may be variable. Mucinous adenocarcinoma may infiltrate locally and extend into the orbit. Treatment involves wide resection with frozen sections (Shields and Shields 1999; Albert and Jakobiec 2008).

Differential Diagnosis

Apocrine hidrocystoma
Cylindroma
Syringoma
Eccrine spiradenoma
Eccrine acrospiroma
Eccrine hidrocystoma

Management

See individual entities for further information.

Cross-References

- ▶ Cylindroma
- ▶ Eccrine Acrospiroma
- ▶ Eccrine Spiradenoma
- ▶ Hidrocystoma, Apocrine
- ▶ Porosyringoma

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Swinging Flashlight Test

▶ Swinging-Light Test, for RAPD Identification

Swinging-Light Test, for RAPD Identification

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Synonyms

Alternating Light Test; Gunn Pupillary Test; Swinging Flashlight Test

Definition

The swinging flashlight test is used to detect a relative afferent pupillary defect (RAPD). (see Cross-References).

Basic Characteristics

See ▶ *RAPD* entry.

Cross-References

- ▶ Optic neuritis
- ▶ RAPD (Relative Afferent Pupillary Defect)

Further Reading

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Sylvian Aqueduct Syndrome

- ▶ Dorsal Midbrain (Parinaud) Syndrome, Convergence-Retraction Nystagmus, Eyelid Retraction

Symblepharon

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Definition

Adhesion of the palpebral and bulbar conjunctiva may be either partial or complete. Signs and symptoms include eyelid distortion, exposure keratopathy, conjunctivitis, limitation of ocular motility, diplopia, ankyloblepharon, lagophthalmos, and entropion (External Disease and Cornea 2011).

Etiology

Trauma or diseases such as trachoma, pemphigoid, rosacea, Stevens-Johnson syndrome, and toxic epidermal necrolysis (Garg 2009).

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Sympathetic Nerves/Pathway, Orbit Supplied by

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Structure

Sympathetic innervation of the orbit regulates pupillary dilation, vasoconstriction, hidrosis, and smooth muscle function of the eyelids and orbit. The hypothalamus is the origin for sympathetic activity, from which orbit-bound sympathetic fibers descend through the brainstem before entering the spinal cord to synapse in the ciliospinal center of Budge-Waller located at spinal levels C8-T2. Second-order preganglionic neurons that are destined for the head and neck then exit the spinal cord and travel in the cervical sympathetic chain through the brachial plexus, over the lung apex, to synapse in the superior cervical ganglion, which is located near the angle of the mandible and the bifurcation of the common carotid artery (Black et al. 2012). Third-order postganglionic neurons leave the superior cervical ganglion and ascend within the adventitia of the internal carotid artery, collectively known as the carotid plexus, and enter the cavernous sinus. There, the postganglionic oculosympathetic fibers separate from the carotid plexus and join the ophthalmic division of the trigeminal nerve (V1) to enter the orbit. These fibers run though the superior orbital fissure and merge with the long and short ciliary nerves (derived from the nasociliary branch of V1) before

passing through the ciliary ganglion on their way to innervate the dilator muscle of the iris and the superior tarsal (Müller's) and inferior tarsal muscles. The ciliary ganglion is a tissue mass located behind the eye, which contains three roots: sympathetic, parasympathetic (motor), and sensory. The sympathetic fibers have their cell bodies located in the superior cervical ganglion, so they do not synapse on their passage through the ciliary ganglion (Ropper and Brown 2005; Kardon 2005).

Function

Sympathetic fibers are responsible for innervating the periorbital blood vessels, sweat glands, pupil dilator muscle, ciliary muscle, superior tarsal muscle, inferior tarsal muscle, and orbitalis. At the ciliary body, sympathetics activate beta-2 receptors to stimulate relaxation and an increase in ciliary body size. As the aperture of the ciliary body widens with relaxation, the zonules that connect the periphery of the lens to the ciliary body become tauter and cause the lens to flatten. Thus, when the ciliary body is relaxed, the refractive power of the lens is reduced to optimize for far distance vision. In contrast, a decrease in sympathetic innervation to the ciliary body will lead to increased tone of the ciliary body, more relaxed zonules, and a rounder lens with greater refractive power that is ideal for near vision.

In the upper eyelid, the levator palpebrae is responsible for the majority of eyelid elevation and is innervated by the oculomotor nerve (CN 3). In contrast, motor innervation to superior tarsal muscle is supplied by sympathetic fibers and provides 2 mm of eyelid lift. The analogous structure in the lower eyelid is the inferior tarsal muscle, which is also supplied by sympathetics and arises from the capsulopalpebral fascia.

Clinical Relevance

Interruption of the sympathetic chain at any level along this pathway will produce miosis and ptosis, the most common presenting signs of Horner's syndrome. Additional features of the disorder include elevation of the lower eyelid, anhidrosis, and vasodilation. Central Horner's is caused by lesions to the first- and second-order sympathetic neurons. Injuries can be localized along the sympathetic pathway based on the presence and distribution of anhidrosis. In central Horner's, the face, arm, and trunk will show decreased sweating. This is because the sudomotor and vasomotor fibers to the face separate out at the superior cervical ganglions and thus would not be affected by postganglionic lesions (Kennard and Leigh 2011).

Diagnostic tests for subtle Horner's syndrome include topical cocaine and apraclonidine. The application of topical cocaine blocks reuptake of norepinephrine from the synaptic cleft leading to pupil dilation if the sympathetic innervation is intact. One hour after, two drops of 10% cocaine is applied to both eyes, the normal pupil will dilate more than the Horner's pupil causing an increase in anisocoria.

In contrast, apraclonidine is an adrenergic agonist and causes pupillary dilation in the Horner's pupil. Apraclonidine is a selective alpha-2 adrenergic agonist and has only weak alpha-1 properties. When the sympathetic input to the pupillary dilator muscle is decreased secondary to a lesion, an up-regulation of alpha-1 receptors causes denervation supersensitivity. Thus, the application of topical apraclonidine will dilate the abnormal pupil while the normal pupil is unchanged, effectively causing a reversal of anisocoria.

Topical hydroxyamphetamine is used to distinguish pre- and postganglionic Horner's, as it prompts a release of norepinephrine from intact adrenergic nerve endings causing pupillary dilation. One hour after instillation, dilation of both pupils indicates a lesion of the first- or second-order neuron. However, if the smaller pupil does not dilate, a lesion of the postganglionic neuron is indicated.

Depending on the etiology of the Horner's syndrome, ptosis may not be reversible. In these cases, it can be surgically corrected by shortening the superior tarsal muscle with either the Putterman procedure (conjunctival-Muller's muscle resection) or the Fasanella-Servat procedure (tarsoconjunctival resection) (Guthoff and Katowitz 2010).

Cross-References

- ▶ Ciliary Ganglion
- ▶ Ciliary Muscle
- ▶ Horner's Syndrome

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Syndromatic Hepatic Ductular Hypoplasia

▶ Arteriohepatic Dysplasia (Alagille Syndrome), Retinal Degeneration

Syphilis: Overview

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Synonyms

Cupid's itch; French disease; Lues; Lues venerea; Pox; Sexually transmitted disease; Social disease; Venereal disease

Definition

Syphilis is a chronic infectious disease caused by a spirochete, usually venereal in origin but often congenital. Syphilis can affect almost any body organ if left untreated.

Etiology

Syphilis is caused by the spirochete *Treponema pallidum*. Currently, the main route of transmission is sexual contact with infectious lesions. Other less prevalent routs are congenital transmission from mother to fetus in utero, blood product transfusion, and direct contact of skin breaks with infectious lesions.

Clinical Presentation

Patients with untreated infection may experience four stages of disease. The most common manifestation of primary syphilis is a single painless lesion (chancre) usually on the external genitalia. Lip, mouth, and fingers are less common sites of ulcers. Condylomata lata, painless large fleshy lesions in warm moist body areas, are characteristic of secondary syphilis. Left untreated, secondary syphilis may progress to the subclinical latent stage, in which positive serologic test is the only clue of syphilis. Tertiary syphilis refers to gummatous- or granulomatous-like lesions and cardiovascular syphilis. Central nervous system manifestations such as cognitive dysfunction, motor or sensory deficits, ophthalmic or auditory symptoms, cranial nerve palsies, and meningitis can occur during any stage of syphilis.

Ocular Manifestation of Syphilis

Ocular involvement in syphilis may occur in any stages; however, it typically affects ocular structures in the secondary or tertiary stages. Syphilis usually mimics other diseases, which leads to misdiagnosis and delay in the treatment. Any ocular structure can be affected by syphilis. The most common ocular manifestation in both early and

late syphilis is anterior uveitis. Patients with anterior uveitis typically have ocular symptoms such as ocular pain, redness, and photophobia. Papulosquamous lesions of the eyelids, temporary loss of eyebrows, diffuse papillary conjunctivitis, scleroconjunctivitis, granulomatous or nongranulomatous intraocular inflammation, interstitial keratitis, chorioretinitis, retinal vasculitis, papillitis, and neuroretinitis are other common ocular findings in syphilis. Central nervous system involvement may lead to ocular motor palsies and visual field defects.

Chorioretinitis typically presents during secondary syphilis. Patients usually do not have the complaint of ocular pain, but their visual loss may be very severe. A focal or multifocal chorioretinitis with variable degree of vitritis is the most common manifestation. Syphilitic posterior placoid chorioretinitis is another ocular finding pathognomonic of secondary syphilis. It presents with yellowish confluent lesion at the level of RPE with a faded center and surrounding stippled hyperpigmentation of the RPE. Solitary or multifocal lesions are accompanied by variable amount of vitreous inflammation and may be associated with superficial hemorrhages, retinal vasculitis, disk edema, and serous detachment of the RPE. Healed lesions of chorioretinitis manifest with atrophy of the choroid and the retina, along with areas of hyperpigmentation.

Many patients with syphilis have concurrent HIV infection. These patients experience more rapidly progressive and more extensive ocular disease. Their ocular manifestations are usually bilateral and more common in males. The ophthalmologist should evaluate any HIV-infected patients with uveitis for syphilis infection, because syphilis is the most common bacterial eye infection in HIV-positive patients.

Congenital Syphilis

Common presentations of congenital syphilis are bone and cartilage abnormalities (saddle nose, palatal perforation, saber shins, and frontal bossing), circumoral rhagades, persistent rhinitis, hepatosplenomegaly, jaundice, and pneumonia. The patient may present with Hutchinson triad of interstitial keratitis, eighth nerve deafness, and Hutchinson teeth (notched incisors).

Ocular manifestations of congenital syphilis may present at birth or decades later. The most common ocular finding in early congenital infection is multifocal chorioretinitis, which may lead to bilateral salt-and-pepper fundus appearance. The classic ophthalmic finding in untreated congenital syphilis is bilateral non-ulcerative interstitial keratitis, which develops late in the first decade of life. Stromal infiltration starts within superior sector of the cornea and spreads centrally, if left untreated. Interstitial keratitis may lead to deep stromal neovascularization, which gives the cornea a "salmon patch" appearance. The sequel of interstitial keratitis is corneal thinning, scar formation, and stromal ghost vessels. Other less common ocular manifestations in congenital syphilis include retinal vasculitis, optic neuritis, glaucoma, and congenital cataract.

Diagnosis

Dark-field microscopy of glass slides prepared after abrading the active chancre is the most specific technique for diagnosing syphilis. Nontreponemal tests, including rapid plasma reagin (RPR) and venereal disease reference laboratory (VDRL), are routinely used for screening syphilis, although it has false-positive in case of pregnancy, autoimmune disorders, and infections. Treponemal-specific tests, including the enzyme immunoassay, the *T. pallidum* hemagglutination test, the microhemagglutination test, the fluorescent treponemal antibody-absorption test, and the enzyme-linked immunosorbent assay, are used to confirm the diagnosis. False-positive results can occur in case of systemic lupus erythematosus or Lyme disease. Unlike treponemal tests, which remain reactive for life, nontreponemal tests may become nonreactive with effective treatment. Patients suspicious to have neurosyphilis should have a cerebrospinal fluid examination. Positive nontreponemal test in the cerebrospinal fluid examination is in favor of neurosyphilis.

Differential Diagnosis

Differential diagnoses of syphilitic chancre are condyloma acuminata, drug eruptions, genital warts, granuloma inguinale, genital herpes simplex, herpes zoster, HIV disease, lymphogranuloma venerum, urinary tract infection, and varicella-zoster virus. Interstitial keratitis may occur with infectious agents such as mycobacterium tuberculosis, leishmania, *Borrelia burgdorferi*, and Epstein-Barr virus. Necrotizing syphilitic retinitis associated with one or more yellow-white patches of necrosis, vasculitis, vitreous inflammation, and discrete anterior segment inflammation closely mimics acute herpetic retinal necrosis syndrome (Gupta et al. 2009). To make the critical diagnosis of acute syphilitic posterior chorioretinitis, the ophthalmologist should rule out acute posterior multifocal placoid pigment epitheliopathy and atypical serpiginous choroidopathy (Ryan et al. 2013).

Prophylaxis

Using a condom during vaginal, oral, and anal sex may protect from transmission of the infection from skin lesions.

Therapy

Injectable benzathine penicillin G is drug of choice for the treatment of primary, secondary, latent, and tertiary syphilis. Crystalline penicillin G (18–24 million units per day for 10–14 days) is recommended for neurosyphilis and syphilitic uveitis. Alternatives for patients with allergy to penicillin and ocular syphilis are ceftriaxone or chloramphenicol (Skuta 2010).

Prognosis

With penicillin treatment, primary, secondary, and early latent syphilis can be cured successfully. Antibiotics treatment will not repair any organ damage in later stages. Involvement of central nervous system in tertiary syphilis has a very high mortality rate. Maternal syphilis can cause miscarriage and stillbirth. Keratitis, arthritis, deafness, and central nervous system damage may cause severe morbidity for patients with congenital syphilis.

Epidemiology

Syphilis accounts for less than 0.5% of new patients in a referral eye care practice and 0.05% of general ophthalmic outpatients (Krachmer et al. 2011). Concomitant HIV and syphilis infections are prevalent among men who have sex with men and injection drug users. Primary, secondary, and congenital syphilis have been diagnosed more in the past decade (Mattei et al. 2012). Syphilis coinfection with human immunodeficiency virus has also become more common (Mattei et al. 2012).

Cross-References

- ▶ Cataract, Causes and Treatment
- ▶ Herpes Simplex Virus
- ▶ Other Uveitic Etiologies
- ▶ Primary Intraocular Lymphoma
- ▶ Sixth Nerve Palsies

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Syphilitic Keratitis

- ▶ Interstitial Keratitis

T

T1

▶ T1-Weighted Image

T1 Image

▶ T1-Weighted Image

T1 Magnetic Resonance Image (MRI)

▶ T1-Weighted Image

T1 Sequence

▶ T1-Weighted Image

T1-Weighted Image

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Synonyms

T1; T1 image; T1 magnetic resonance image (MRI); T1 sequence; T1WI

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Definition

A T1-weighted (T1W) image is a basic pulse sequence in magnetic resonance (MR) imaging and depicts differences in signal based upon intrinsic T1 relaxation time of various tissues. Clinically, T1-weighted images generally are better for depicting normal anatomy and can accentuate pathology when gadolinium contrast is provided (Damadian 1971; Bitar et al. 2006). For example, fat demonstrates high signal intensity on T1-weighted images, while fluid demonstrates low signal intensity (Bitar et al. 2006). The fat can be suppressed on T1W MRI using fat saturation techniques to allow pathologic T1W hyperintensity to be seen in the orbit without the normal signal created by normal orbital fat.

Basic Characteristics

Physics Fundamentals

The physics of MR imaging are complex and beyond the scope of this chapter, but the concepts required to understand the acquisition and formation of a T1-weighted image will be explained in brief. MR imaging is based on the electromagnetic activity of atomic nuclei (Bitar et al. 2006). These nuclei are made up of protons and neutrons, which have spins. MR-active nuclei are those with a net spin because they are odd numbered and the spins of their protons and neutrons do not cancel each other out (Bitar et al. 2006). In clinical MR imaging, hydrogen (^{1}H) nuclei are used most often because of their abundance in the body (Bitar et al. 2006). Thus, it is necessary to have a source of hydrogen protons (protons in the nuclei of hydrogen atoms, which are associated with fat and water molecules) in order to form an MR signal (Pooley 2005). The hydrogen proton is positively charged and spins about its axis (like a child's spinning top). This positively charged spinning proton acts like a tiny magnet; the hydrogen protons in our body thus act like many tiny magnets (Pooley 2005).

A strong magnetic field is applied in MR imaging, and the main magnetic field of an MR system comes from a large electric current flowing through wires that are formed into a loop in the magnet of the imaging system (Pooley 2005). A typical clinical MR system has a magnetic field strength of 1.5 tesla (T) or 3.0 T, but higher strength magnets are becoming increasingly developed.

Putting these concepts together, there are protons in the body, positively charged and spinning about their axes, and acting like tiny magnets (Pooley 2005). When these protons are placed in a strong magnetic field (so-called B_0), some will tend to align in the direction of the magnetic field, and others will align opposite to the magnetic field. The magnetic fields from most of these protons will cancel out, but a slight excess of protons will align with the main magnetic field (Pooley 2005). The cumulative effect of all the magnetic moments of the nuclei is the "net magnetization" vector that is aligned parallel to the main magnetic field (Pooley 2005; Bitar et al. 2006).

This net magnetization becomes the source of our MR signal and is used to produce MR images (Pooley 2005). The way this works is that once net magnetization is achieved, a radiofrequency (RF) pulse is applied (a component of the MR scanner), causing the net magnetization vector to flip by a certain angle, producing two magnetization vector components, longitudinal and transverse magnetization (Bitar et al. 2006). The transverse component of the net magnetization vector induces a current in the receiver coil (another component of the MR scanner). This current ultimately becomes the MR signal (Bitar et al. 2006).

When the RF energy source is turned off, the net magnetization vector realigns with the axis of B_0 through the process of T1 recovery, during which the longitudinal magnetization increases in magnitude, or recovers (Bitar et al. 2006). Simultaneously, the transverse magnetization decreases (decays) through additional mechanisms known as T2* and T2 decay (Bitar

et al. 2006). Different tissues have different characteristic T1, T2, and T2* values, which is in large part what allows the differentiation of tissues and disease processes in clinical imaging. Fat has a shorter T1 (i.e., recovers faster) and a shorter T2 (i.e., decays faster) than water, which has a relatively long T1 and T2. T2* decay occurs very quickly in both fat and water (Bitar et al. 2006). Tissues with an inherently short T1 time appear bright on T1-weighted images (such as fat), while tissues with a long T1 time will appear dark (such as air) (Hathout 2009). Along the same lines, tissues with a long T2 time will appear bright on T2-weighted images (such as water), while tissues with a short T2 time will appear dark (such as the cortical bone).

On a final technical note, two key parameters – repetition time (TR) and echo time (TE) – are key to the creation of image contrast (Bitar et al. 2006). While further discussion of these values is beyond the scope of this chapter, TR and TE can be adjusted to emphasize a particular type of contrast (i.e., T1, T2). T1 weighting is produced by utilizing short TR and TE times. In T1-weighted MR imaging, while images show all types of contrast, T1 contrast is accentuated (Bitar et al. 2006).

Uses for T1 Weighting

Clinically, T1-weighted images best depict anatomy and can accentuate pathology when contrast is provided (Damadian 1971; Bitar et al. 2006). As stated previously, with MR imaging only hydrogen protons are visualized. The MR imaging contrast agent most frequently utilized is gadolinium. Gadolinium is a paramagnetic material that produce "contrast enhancement" by shortening the T1 time of hydrogen protons in their vicinity, thus causing them to appear bright on T1-weight MR images, in just the same fashion that protons within intrinsically short T1 time constants, such as hydrogen protons in fat, are bright on T1-weighted MR imaging (Hathout 2009). A smaller concentration of gadolinium is required to achieve this T1 shortening in MR imaging than the concentration of iodine needed to achieve appreciable increases in density on contrast CT examinations. Thus, a mass may appear as non-enhancing on contrast CT, yet as avidly enhancing on contrast MR imaging (Hathout 2009).

T2-weighted images, on the other hand, provide the best depiction of disease, because most tissues involved in a pathologic process have a higher water content than normal, and fluid causes affected areas to appear bright on T2-weighted images (Bitar et al. 2006). In regard to neuroimaging, white matter has a very short T1 time and relaxes rapidly; cerebrospinal fluid (CSF) has a long T1 and relaxes slowly. Gray matter has an intermediate T1 and relaxes at an intermediate rate (Pooley 2005). If an image were created at a time when the T1 curves for these tissues were widely separated, an image with high contrast between these tissues would be formed. White matter contributes to brighter pixels, CSF contributes to darker pixels, and gray matter contributes to pixels with intermediate shades of gray; this type of contrast mechanism is termed T1-weighted contrast (Pooley 2005). A summary of the appearance of various tissues on T1-weighted images is provided below (Bitar et al. 2006) Table 1.

T1-Weighted Image, Table 1 Appearance of tissues on T1-weighted images

Signal intensity	Tissues
Dark	Air, mineral-rich tissue (cortical bone, stones), fast-flowing blood
Low	Collagenous tissue (ligaments, tendons, scars), high free water tissue (kidneys, gonads, edema, fluids [urine, bile], simple cysts, bladder, gallbladder, spleen, CSF), high bound-water tissues (liver, pancreas, adrenals, hyaline cartilage, muscle)
Intermediate	Proteinaceous tissue (abscess, complex cysts, synovial fluid)
Bright	Fat, fatty bone marrow, blood products (methemoglobin, slow-flowing blood, radiation change, paramagnetic contrast agents)

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T1WI

▶ T1-Weighted Image

T2

▶ T2-Weighted Image

T2 Image

▶ T2-Weighted Image

T2 Magnetic Resonance Image (MRI)

▶ T2-Weighted Image

T2 Sequence

▶ T2-Weighted Image

T2-Weighted Image

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Synonyms

T2; T2 image; T2 magnetic resonance image (MRI); T2 sequence; T2WI

Definition

A T2-weighted image is a basic pulse sequences in magnetic resonance (MR) imaging that depicts differences in the T2 relaxation time of various tissues. Clinically, T2-weighted images provide the best depiction of disease, because most tissues involved in a pathologic process have a higher water content than normal, and fluid (e.g., cerebrospinal fluid, vitreous humor) causes affected areas to appear bright on T2-weighted images (Bitar et al. 2006).

Basic Characteristics

Physics Fundamentals

The physics of magnetic resonance (MR) imaging are complex and beyond the scope of this chapter,

but the concepts required to understand the acquisition and formation of a T2-weighted image will be explained in brief. MR imaging is based on the electromagnetic activity of atomic nuclei (Bitar et al. 2006). These nuclei are made up of protons and neutrons, which have spins. MR-active nuclei are those with a net spin because they are odd numbered, and the spins of their protons and neutrons do not cancel each other out (Bitar et al. 2006). In clinical MR imaging, hydrogen (^{1}H) nuclei are used most often because of their abundance in the body (Bitar et al. 2006). Thus it is necessary to have a source of hydrogen protons (protons in the nuclei of hydrogen atoms, which are associated with fat and water molecules) in order to form an MR signal (Pooley 2005). The hydrogen proton is positively charged and spins about its axis (like a child's spinning top). This positively charged spinning proton acts like a tiny magnet; the hydrogen protons in our body thus act like many tiny magnets (Pooley 2005).

It is also a prerequisite to apply a magnetic field in MR imaging; the main magnetic field of an MR system comes from a large electric current flowing through wires that are formed into a loop in the magnet of the imaging system (Pooley 2005). A typical clinical MR system has a magnetic field strength of 1.5 tesla (T) or 3.0 T.

Putting these concepts together, there are protons in the body, positively charged and spinning about their axes, acting like tiny magnets (Pooley 2005). When these protons are placed in a strong magnetic field (so-called B_0), some will tend to align in the direction of the magnetic field and others will align opposite to the magnetic field. The magnetic fields from most of these protons will cancel out, but a slight excess of protons will align with the main magnetic field (Pooley 2005). The cumulative effect of all the magnetic moments of the nuclei is the "net magnetization" vector that is aligned parallel to the main magnetic field (Pooley 2005; Bitar et al. 2006).

So how does this relate to the images we are used to seeing in clinical practice? This net magnetization becomes the source of our MR signal and is used to produce MR images (Pooley 2005). The way this works is that once net magnetization is achieved, a radiofrequency (RF) pulse is applied (a component of the MR scanner), causing the net magnetization vector to flip by a certain angle, producing two magnetization vector components, longitudinal and transverse magnetization (Bitar et al. 2006). The transverse component of the net magnetization vector induces a current in the receiver coil (another component of the MR scanner). This current ultimately becomes the MR signal (Bitar et al. 2006).

When the RF energy source is turned off, the net magnetization vector realigns with the axis of B_0 through the process of T1 recovery, during which the longitudinal magnetization increases in magnitude, or recovers (Bitar et al. 2006). Simultaneously, the transverse magnetization decreases (decays) through additional mechanisms known as T2* and T2 decay (Bitar et al. 2006). Different tissues have different characteristic T1, T2, and T2* values, which are in large part what allow the differentiation of tissues and disease processes in clinical imaging. Fat has a shorter T1 (i.e., recovers faster) and a shorter T2 (i.e., decays faster) than water, which has a relatively long T1 and T2. T2* decay occurs very quickly in both fat and water (Bitar et al. 2006). Tissues with an inherently short T1 time appear bright on T1-weighted images (such as fat), while tissues with a long T1 time will appear dark (such as air) (Hathout 2009). Along the same lines, tissues with a long T2 time will appear bright on T2-weighted images (such as water), while tissues with a short T2 time will appear dark (such as cortical bone).

On a final technical note, two key parameters – repetition time (TR) and echo time (TE) – are key to the creation of image contrast (Bitar et al. 2006). While further discussion of these values is beyond the scope of this chapter, TR and TE can be adjusted to emphasize a particular type of contrast (i.e., T1, T2). T2 weighting is produced by utilizing long TR and TE times (Bitar et al. 2006).

Uses for T2 Weighting

Clinically, T2-weighted images provide the best depiction of disease, because most tissues

involved in a pathologic process have a higher water content than normal, and fluid causes affected areas to appear bright on T2-weighted images (Bitar et al. 2006). This is in contrast to T1-weighted images, which best depict anatomy and can accentuate pathology when contrast is provided (Damadian 1971; Bitar et al. 2006). In regard to neuroimaging, white matter has a short T2 and dephases rapidly; cerebrospinal fluid (CSF) has a long T2 and dephases slowly (Pooley 2005). Gray matter has an intermediate T2 and dephases intermediately. Clinically these differences can be taken advantage of, and images based on this contrast mechanism may be produced, called "T2-weighted contrast" (Pooley 2005). If an image were created at a time when transverse magnetization curves were widely separated, then high contrast between the tissues would be obtained. CSF would be associated with brighter pixels, white matter with darker pixels, and gray matter with intermediately gray-level pixels (Pooley 2005). A summary of the appearance of various tissues on T2-weighted images is provided below (Bitar et al. 2006) (Table 1).

T2-Weighted Image, Table 1 Appearance of tissues on T2-weighted images

Signal intensity	Tissues
Dark	Air, mineral-rich tissue (cortical bone, stones), fast-flowing blood
Low	Collagenous tissue (ligaments, tendons, scars), bone islands
Low to intermediate	High bound water tissues (liver, pancreas, adrenals, hyaline cartilage, muscle)
Intermediate to bright	Fat, fatty bone marrow
Bright	High free water tissue (kidneys, gonads, edema, fluids [urine, bile], simple cysts, bladder, gallbladder, spleen, CSF). Proteinaceous tissue, blood products (oxyhemoglobin, extracellular methemoglobin)

Cross-References

► T1-Weighted Image

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T2WI

► T2-Weighted Image

Tablets

► Ketorolac Tromethamine

Tamsulosin

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Synonyms

Flomax™

Definition

Selective alpha-1 adrenergic blocker.

Indication

Management of lower urinary tract symptoms in men with moderate to severe urinary symptoms due to benign prostatic hyperplasia.

Contraindication

Tamsulosin capsules are contraindicated in patients known to be hypersensitive to tamsulosin hydrochloride or any component of tamsulosin capsules.

Use and Dosage

Tamsulosin 0.4 mg once daily is recommended as the dose for the treatment of the signs and symptoms of benign prostatic hyperplasia. For those patients who fail to respond to the 0.4 mg dose after 2–4 weeks of dosing, the dose of tamsulosin can be increased to 0.8 mg once daily.

Adverse Reactions

Intraoperative floppy iris syndrome in cataract surgery is strongly correlated with systemic use of tamsulosin. The syndrome consists of poor pupillary dilation, progressive intraoperative miosis with billowing of the iris, and increased risk of iris prolapse through the corneal incisions and is therefore associated with increased risks of surgical complications. Therefore, the use of pupil dilators should be considered in patients with a history of tamsulosin medication. The deleterious effects of tamsulosin on cataract surgery can persist for years after discontinuation. The signs and symptoms of orthostasis (postural hypotension, dizziness, and vertigo) are detected more frequently in tamsulosin-treated patients. As with other alpha-adrenergic blocking agents, there is a potential risk of syncope.

Interactions

Doses of tamsulosin higher than 0.4 mg (e.g., 0.8 mg) should not be used in combination with strong inhibitors of CYP3A4 (e.g., ketoconazole).

Cross-References

- ▶ Cataract Surgery
- ▶ Intraoperative Floppy-Iris Syndrome
- ▶ Pupil Dilator

Further Reading

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Tangier Disease, Corneal Changes

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Synonyms

Familial alpha-lipoprotein deficiency; Hypoalphalipoproteinemia

Definition

Bilateral stromal opacities in the setting of Tangier disease.

Etiology

A defect in the ABCA1 cellular membrane transporter in Tangier disease prevents adequate removal of cholesterol from cells. Cholesterol and phospholipid esters accumulate over time in the corneal stroma due to its relatively low temperature and lack of vascularity. The disease is inherited in an autosomal recessive fashion due to mutations in the ABCA1 gene in chromosome 9q31.

Clinical Presentation

Corneal changes in Tangier disease appear as bilateral corneal opacifications limited to the stroma and generally present in adult life. Deposits appear small and granular, distributed with relatively similar density through the anterior and posterior stroma. Although the rarity of cases prevents generalization, early findings may involve increased density in the nasal and temporal quadrants, later involving the paracentral and peripheral cornea. Endothelial cell density is not affected. Patients may also demonstrate conjunctival perivascular deposits. Decrease in visual acuity may correlate with opacification and is variable, ranging from relatively mild to marked visual impairment. Comorbidities reported include keratitis, ectropion, and incomplete eye closure, but an association with Tangier disease is unclear.

Diagnosis

Serum lipid analysis reveals minimal levels of high-density lipoproteins (HDL), and genetic analysis for the ABCA1 mutation can confirm the presence of Tangier disease. Slit-lamp biomicroscopy should be utilized to identify and localize the presence of corneal opacities. Conjunctival biopsy shows birefringent lipid particles in vascular pericytes but is generally not required for diagnosis. Detailed medical and surgical history should be acquired, with consideration for systemic associations, including yellow-orange tonsils, splenomegaly, hepatomegaly, cardiovascular disease, and neuropathy.

Differential Diagnosis

The differential diagnosis for bilateral stromal opacities includes ▶ Schnyder corneal dystrophy, ▶ lipid keratopathy, and ▶ corneal arcus; HDL deficiencies such as lecithin-cholesterol acyltransferase deficiency and fish eye disease; and other crystalline deposits such as cystinosis, gout, mucolipidosis, and mucopolysaccharidosis. Tangier disease is marked by its autosomal recessive transmission, unlike Schnyder corneal dystrophy which is autosomal dominant.

Prophylaxis

No method of prophylaxis is known at this time.

Therapy

Mild opacities may be observed. Corneal transplantation can be considered for severe cases, with option of either deep anterior lamellar keratoplasty or penetrating keratoplasty, although outcomes are unclear. Patients should undergo systemic evaluation and treatment of lipid abnormalities.

Prognosis

Visual acuity ranges from mildly to severely affected, correlates with corneal opacities, and slowly decreases over years to decades.

Epidemiology

Rare. First described in a patient from Tangier Island, Virginia, approximately 50 cases have been identified globally. The prevalence of corneal changes among these patients is unclear.

Cross-References

- ▶ Corneal arcus
- ▶ Lipid keratopathy
- ▶ Mucopolysaccharidosis
- ▶ Schnyder Crystalline Dystrophy Syndrome

Further Reading

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Tanning Pills Retinopathy

- ▶ Canthaxanthin, Retinopathy

Tarsal Conjunctiva

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Synonyms

Palpebral conjunctiva

Definition

The conjunctiva proper is a translucent mucous membrane covering the anterior surface of the eye and posterior side of the eyelid. The conjunctiva becomes continuous with the corneal epithelium. The conjunctiva can be divided into the palpebral conjunctiva, fornices, and bulbar conjunctiva. Specifically, the palpebral conjunctiva lines the posterior surface of the eyelid.

Structure

The palpebral conjunctiva can be subdivided into the marginal, tarsal, and orbital conjunctiva (Goldman 2011).

The marginal conjunctiva posteriorly and the skin anteriorly form the surface of the eyelid margin. The transition zone between these structures is known as a mucocutaneous junction. The marginal conjunctiva is continuous with the tarsal conjunctiva and more inferiorly the sub-tarsal sulcus.

The tarsal conjunctiva is a vascular structure tightly adherent to the tarsal plates in both upper and lower eyelids (Goldman 2011).

The orbital conjunctiva is a loose covering between the tarsal plate and the fornix, lying over the Muller's muscle in the upper eyelid and the lower lid retractors in the lower eyelid.

Function

The palpebral conjunctiva contains accessory lacrimal glands and goblet cells producing tears and mucus, respectively, contributing to the maintenance of the healthy pre-corneal tear film. It is also critical for proper function of the specialized sebaceous glands of the tarsus, meibomian glands, which contribute to the lipid layer of the tear film. It serves as a reservoir for tears and provides oxygen to the cornea. The palpebral conjunctival also contributes to immune surveillance and forms a protective barrier over the anterior portion of the globe (Takahashi et al. 2013).

Clinical Relevance

The sub-tarsal sulcus is a common site for foreign body lodgement (Fonolla et al. 2001). Furthermore, the palpebral conjunctiva represents an area where reactive pathology of the conjunctiva can be seen. Follicle formation occurring in the palpebral conjunctiva is associated with viral and chlamydial infections, as well as toxic conjunctivitis

(Pacharn et al. 2013). Papillae formation within the palpebral conjunctiva is associated with allergic diseases, but can also be associated with non-pathological conditions such as prolonged contact lens use (Pacharn et al. 2013). Many cicatrizing and inflammatory conditions such as Steven's Johnson's syndrome or ocular cicatricial pemphigoid affect the palpebral conjunctiva. These processes can lead to entropion, forniceal shortening, and trichiasis, with eventual corneal scarring and blindness (Chiou et al. 1998). Multiple surgical incisions used to gain entrance to the orbit and eyelids are performed through the palpebral conjunctiva to camouflage the scar (Goldman 2011).

Cross-References

▶ Palpebral Conjunctiva

References

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Tarsal Fracture Operation, for Cicatricial Entropion

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Synonyms

Transverse tarsotomy with lid margin rotation

Definition

The tarsal fracture operation refers to a surgical procedure where the eyelid tarsus is iatrogenically fractured with a full-thickness tarsal incision, allowing for independent rotation of both segments of the eyelid above and below the incision, which can be utilized in the surgical repair of eyelid malposition.

Indication

The tarsal fracture operation is indicated for the surgical repair of mild to moderate cicatricial entropion (Bercovici et al. 1977; Kersten et al. 1992). A full-thickness incision through the tarsus is made from the posterior or conjunctival aspect of the eyelid "fractures" or mechanically dissociates the superior and inferior portions of the tarsus and allows the eyelid to "bend." In the case of entropion, the eyelid margin is everted or bent away from the globe with the use of everting sutures. External rotation of the eyelid margin redirects eyelashes away from the cornea and globe, reducing the incidence of ocular surface irritation, keratopathy, epithelial defects, corneal ulcers, and even corneal perforation

Contraindication

The tarsal fracture operation is not usually performed in cases of involutional entropion where chronic tarso-conjunctival inflammation and cicatrisation are not present. Other contraindications to the tarsal fracture operation, which is usually performed under general anesthesia, are mostly related to the general medical condition and operative risk of the patient. The tarsal fracture procedure may be contraindicated in patients with concurrent uncontrolled medical conditions, systemic anticoagulation, or other conditions that interfere with appropriate positioning or safe management of the patient in the operating room. In such situations, simpler less invasive methods of eyelid malposition correction such as the Quickert

procedure for entropion may be preferred, even if they may be associated with higher long-term recurrence.

Techniques and Principles

1. After skin preparation, infiltrate locally administered anesthetic agent subcutaneously and subconjunctivally along the lower border of the inferior tarsus or superior border of the superior tarsus.
2. Stabilize the eyelid by placing a 4-0 silk traction suture through the eyelid margin, and evert the eyelid using a Jaeger lid speculum, exposing the posterior conjunctival aspect of the eyelid.
3. Using a 15 blade, fashion a horizontal full-thickness tarsal incision from the conjunctival aspect 2 mm inferior to the eyelid margin in the lower lid, or 2 mm superior to the eyelid margin in the upper lid.
4. Place 2-3 Quickert everting sutures to fixate and rotate the eyelid margin away from the globe

Outcome

A retrospective review of the tarsal fracture operation reported a favourable outcome rate of in 94% of cases of mild to moderate cicatricial entropion. The same study found a lower success rate of 55% in cases of severe cicatricial entropion (Kersten et al. 1992). Several studies have reported that overall success rates increase after reoperations in cases of recurrence, even in severe cases, suggesting that tarsal fracture may still be considered as an acceptable procedure in the initial management of severe cicatricial entropion (Kersten et al. 1992; Pombejara and Tirakunwichcha 2011).

Other techniques reported for the surgical management of severe cicatricial entropion include posterior lamellar eyelid reconstruction techniques with the use of tissue grafts. Additional tissue used in these techniques aids with improving outcomes and reducing recurrence. Buccal, hard palate, and nasal turbinate mucosa have been used as donor graft tissue for posterior buttress eyelid reconstruction (Bartley and Kay 1989; Goldberg et al. 1999). In these studies, successful treatment of eyelid malposition was achieved in 86% of patients.

Complications

The tarsal fracture operation is a relatively simple operation. Complications of the tarsal fracture operation include failure of entropion correction, recurrence, ectropion overcorrection, granuloma formation, infection, bleeding, and wound dehiscence. Careful burying of deep sutures while minimizing dead space aids in the reduction of suture granuloma formation and suture extrusion. Attention to appropriate surgical technique, good placement of sutures, and secure knots maximizes the chances of surgical success. Avoidance of trauma in the postoperative period, good patient hygiene, and use of topical antibiotic ointment may also contribute to minimizing complications. Patients should also be counselled by the anesthesiologist regarding the risks and complications of general anesthesia.

Cross-References

- ▶ Botox: Spastic Entropion
- ▶ Melanoma of the Eyelid
- ▶ Sutures (Surgical), Quickert, for Involutional Entropion
- ▶ Wies Repair

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Tarsal Glands

► Meibomian Glands

Tarsal Kink

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Synonyms

Congenital entropion

Definition

Tarsal kink is a form of congenital entropion characterized by a horizontal fold in the tarsus along the inferior third of the upper eyelid.

Etiology

The etiology of tarsal kink is unclear but possibilities include a primary tarsal defect, an aponeurotic defect, overacting orbicularis fibers, an exogenous mechanical force in utero, or an eyelid disjunction defect in utero.

Clinical Presentation

Tarsal kink presents as a unilateral or bilateral upper eyelid entropion at birth. It is usually associated with marked blepharospasm and an absent lid crease. Corneal ulceration is present in roughly half of patients.

Diagnosis

Diagnosis of tarsal kink is made clinically. Associated corneal ulcers, present in roughly half of patients, may be cultured. The most common causative organisms are *S. Aureus* and *S. Epidermidis*.

Differential Diagnosis

Congenital entropion without tarsal kink

Therapy

Treatment of tarsal kink involves "unfolding" of the kink by patching or surgical rotation. In general, surgical procedures are geared towards weakening the kink, rotating it with sutures, and closing with supratarsal fixation to re-form the eyelid crease. Surgical procedures include suture rotation over bolsters, full-thickness horizontal kink excision, skin and muscle excision or repositioning, tarsal excision with suture rotation, lamellar tarsectomy with flip, and tarsal incision with suture rotation and supratarsal fixation.

Prognosis

The majority of patients will continue to have normal visual development following tarsal kink repair. Factors leading to poor visual outcomes include the presence of an ulcer or a delay in diagnosis.

Epidemiology

Rare

Cross-References

▶ Congenital Entropion

Further Reading

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Tarsal Muscles, Inferior

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Synonyms

Inferior tarsal muscle

Definition

The inferior tarsal muscle and the capsulopalpebral fascia make up the lower eyelid retractors.

Structure

The lower eyelid retractors include the inferior tarsal muscle and the capsulopalpebral fascia, both of which attach to the tarsal plate. The inferior tarsal muscle is innervated by the sympathetic nervous system and gets its blood supply from the inferior palpebral artery. The capsulopalpebral fascia originates from the inferior rectus muscle fascia and wraps anteriorly around the inferior oblique muscle to reach the Lockwood ligament. From here the capsulopalpebral fascia courses forward to reach the lower margin of the tarsus and the subcutaneous tissue. Running deep to the capsulopalpebral fascia is the inferior tarsal muscle. The inferior tarsal muscle is approximately half the size of the superior tarsal muscle (4–5 mm vs. 9–10 mm), but both are similar in length and thickness, and both are lined posteriorly with densely adherent conjunctiva (Sand et al. 2016).

Function

The inferior tarsal muscle helps in lower eyelid retraction.

Clinical Relevance

Disruption in lower eyelid retractors can cause entropion and ectropion, where the lower eyelid is folded inward toward the eye or outward from the eye, respectively (Kakizaki et al. 2009). These conditions occur more readily with disruption of the capsulopalpebral fascia, since this serves as the primary lower lid retractor. Disrupting the inferior tarsal muscle alone may cause eyelid malposition, but is not classically seen in patients.

Knowledge of lower eyelid retractors is needed for successful outcomes in cosmetic and reconstructive lower eyelid surgery. When the lower eyelid retractors are the targets of certain eyelid malposition surgeries, the surgeon should carefully look for the retractors in the posterior layer, which is where the main retractional component lies. Appropriate advancement of the posterior layer may provide good outcomes in lower eyelid entropion surgery, or occasionally in ectropion surgery in the absence of retraction.

Cross-References

▶ Capsulopalpebral Fascia
▶ Tarsal Plates/Tarsus

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Tarsal Plate

► Tarsal Plates/Tarsus

Tarsal Plates/Tarsus

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Synonyms

Tarsal plate; Tarsoligamentous sling; Tarsus

Definition

Fibrous plates providing structural integrity to the upper and lower eyelids

Structure

Recent immunohistochemical studies suggest that the tarsus is a "transitional tissue" with features of both dense fibrous connective tissue and cartilage. It contains fibroblastic cells in an extracellular matrix dominated by type I and III collagen and proteoglycans. Chondrocytes and type II collagen are notably absent. Aggrecan and chondroitin sulfate, however, are present in relative abundance (Milz et al. 2005).

The horizontal dimension of the tarsal plates is slightly narrower than that of the palpebral fissure (25–30 mm) (Bedrossian 2006). Maximum tarsal thickness is approximately 1 mm centrally. Height in the midpupillary axis is 10–12 mm in the upper eyelid and 4–6 mm in the lower eyelid. Approaching the medial and lateral commissures, the plates in both lids taper to a height of 2 mm before merging with the canthal tendons.

The lateral canthal tendon joins with the lateral horn of the levator, lateral rectus check ligament, and Lockwood's ligament to form the lateral retinaculum. This inserts on Whitnall's tubercle, a bony prominence inside the orbital rim. The medial canthal tendon splits to form anterior and posterior limbs. These limbs insert on the anterior and posterior lacrimal crests, respectively, straddling the lacrimal sac within its bony fossa. The accompanying deep heads of the pretarsal and preseptal orbicularis muscle also insert on the posterior lacrimal crest.

Palpebral conjunctiva is firmly adherent to the internal surface of the tarsal plates. Mulller's muscle and capsulopalpebral fascia insert on the respective antimarginal tarsal borders. The levator aponeurosis inserts on the anterior surface of the superior tarsal plate, interdigitating with orbicularis to form the eyelid crease. The pretarsal orbicularis muscle is relatively adherent to the the anterior tarsal plates.

The upper eyelid contains 30–40 meibomian glands, while the lower contains 20–30. The gland orifices are located between the gray line (muscle of Riolan) and eyelid myocutaneous junction.

Function

A fibrous skeleton consisting of the tarsal plates and canthal tendons maintains the structural integrity of the eyelids (the "tarsoligamentous sling"). It keeps the lids closely approximated to the ocular surface and plays a vital protective role. The indwelling meibomin glands are holocrine glands responsible for producing the lipid layer of the precorneal tear film.

Clinical Relevance

Knowledge of tarsal anatomy is crucial for eyelid reconstruction following trauma or Mohs surgery. When using free taral grafts or pedicle flaps (e.g., Hughes), it is important to leave 4 mm of marginal tarsus in the upper lid and 2 mm in the lower lid in order to to avoid destabilization. When portions of tarsus are missing, the cut ends should be trimmed perpendicular to the lid margin in order to prevent notching.

The tarsal plate becomes lax in floppy eyelid syndrome (FES), permitting the lid to evert easily. Histopathological studies demonstrate a decreased abundance of mature elastic fibers (Ezra et al. 2011). Ordinarily, these fibers are principally distributed around the meibomian glands and extend toward the muscle of Riolan (Kakizaki et al. 2011). This dropout may therefore contribute to the abnormal lipid secretion and lash ptosis seen with FES.

Cross-References

- ▶ Chalazion
- ▶ Meibomian Gland Dysfunction
- ▶ Tarsal Conjunctiva
- ▶ Tarsorrhaphy

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Tarsal Strip Procedure

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Synonyms

Lateral tarsal strip procedure

Definition

The tarsal strip procedure refers to the surgical shortening of the lateral canthal tendon or lateral edge of the tarsal plate. The procedure results in a superior and lateral distraction of the lax eyelid.

Indication

The tarsal strip procedure reduces horizontal eyelid laxity and corrects eyelid malposition through direct mechanical shortening of the canthal tendon. The tarsal strip procedure was first described by Anderson and Gordy in 1979 for the surgical repair of paralytic or senile upper or lower eyelid laxity, lateral canthal tendon laxity or malposition, and iatrogenic phimosis associated with recurrent entropion or ectropion (Anderson and Gordy 1979). Since then, the tarsal strip procedure has also been reported to be used in the correction of lax eyelid syndrome, mild post-enucleation socket syndrome, orbital decompression, repair of lateral canthotomy in the swinging eyelid flap for orbital floor implants, lower eyelid transcutaneous or trans-conjunctival blepharoplasty, sub-orbicularis oculi fat pad (SOOF) lift, and cicatrical ectropion when combined with a free skin graft (Olver 1998).

Recently, the tarsal strip procedure has been increasingly combined with Quickert everting sutures, which aids with eyelid eversion in the

surgical management of eyelid entropion (Ho et al. 2005). This procedure, described as a lateral tarsal strip with everting sutures, has been described and shown to be an effective and simple procedure suitable for use by a comprehensive ophthalmologist.

Contraindication

Contraindications to the tarsal strip procedure, which is usually performed under general anesthesia, are mostly related to the general medical condition and operative risk of the patient. The tarsal strip procedure may be contraindicated in patients with concurrent uncontrolled medical conditions, systemic anticoagulation, or other conditions that interfere with appropriate positioning or safe management of the patient in the operating room. In such situations, simpler less invasive methods of eyelid malposition correction such as the Quickert procedure for entropion may be preferred, even if they may be associated with higher long-term recurrence.

Techniques and Principles

The tarsal strip procedure is performed as follows:

1) After skin preparation, infiltrate locally administered anesthetic agent subcutaneously and subconjunctivally along the lateral periorbital region.
2) Use a blade to make a 0.5–1.0 cm superficial skin-orbicularis incision along a skin crease, exposing the fascia overlying the periosteum of the lateral orbital rim.
3) Perform an upper or lower limb lateral canthotomy and cantholysis, depending on which eyelid surgery is intended upon.
4) Split the anterior and posterior lamellae of the eyelid along the gray line by an extent to which eyelid shortening is desired.
5) Excise the anterior mucocutaneous junction of the strip and excess skin using scissors.
6) De-epithelialize the tarso-conjunctival epithelium with gentle cautery and scraping with a blade.
7) Secure the tarsus to the lateral orbital rim using nonabsorbable 5-0 Prolene sutures.
8) Close the orbicularis and skin layers separately with 6-0 and 8-0 Vicryl sutures respectively.

Outcome

The tarsal strip procedure is an effective surgical procedure for the correction of eyelid malposition. A clinical series of tarsal strip procedures reported a 92–95% rate of success with few complications (Riedel and Beyer-Machule 1991). The tarsal strip procedure with everting suture procedure used in involutional entropion has been reported to have recurrence rates of 2–9.4% (Olver 1998; Ho et al. 2005). Horizontal or vertical eyelid laxity, eyelid retractor attenuation or disinsertion, and overriding of the preseptal orbicularis oculi are three main components leading to involutional entropion. Effective surgical repair of involutional entropion often involves correction of at least two of the three main components of entropion, and the tarsal strip procedure reduces both horizontal eyelid laxity and retractor attenuation.

In addition to the effectiveness in correcting eyelid malposition, the tarsal strip procedure maintains the natural anatomic configuration of the lateral canthal angle, which translates to excellent cosmetic results. The procedure is relatively simple and minimally invasive compared to other eyelid malposition surgical procedures that involve full-thickness wedge resections, which leads to a favorable postoperative recovery course.

Complications

Complications of the tarsal strip procedure include conjunctival cysts, granuloma formation, suture extrusion, infection, bleeding, slippage of lateral canthal tendon, and wound dehiscence. Cautery of the tarsoconjunctival epithelium ablates epithelial and mucin-producing Goblet cells, reducing the rate of conjunctival cyst formation. Careful burying of deep sutures while minimizing dead space aids in the reduction of suture granuloma formation and suture extrusion.

Attention to appropriate surgical technique, good placement of sutures, and secure knots reduces the occurrence of tendon slippage and wound dehiscence. Avoidance of trauma in the postoperative period, good patient hygiene, and use of topical antibiotic ointment may also contribute to minimizing complications.

Cross-References

- ▶ Congenital Entropion
- ▶ Melasma, of Eyelids
- ▶ Sutures (Surgical), Quickert, for Involutional Entropion
- ▶ Wies repair

References

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Tarsal Substitute

- ▶ Hard Palate Graft

Tarsoconjunctival Graft

- ▶ Hughes Procedure/Modified Hughes Procedure, in Eyelid Repair

Tarsoligamentous Sling

- ▶ Tarsal Plates/Tarsus

Tarsorrhaphy

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Synonyms

Temporary suture tarsorrhaphy (TST)

Definition

A surgical procedure designed to protect the ocular surface by narrowing or closing the palpebral aperture.

Indication

Central tarsorrhaphies are generally a temporary measure to treat non-healing epithelial defects and neurotrophic ulcers. They may also be required in critically ill, intubated patients with lagophthalmos. Aggressive lubrication and moisture chambers are typically used as primary interventions, but tarsorrhaphy becomes necessary with evidence of progressive exposure keratitis.

Lateral tarsorrhaphies are used to reduce ocular surface evaporation by narrowing the horizontal palpebral aperture. They may be used in patients with facial nerve palsies or other pathologies expected to result in long-term exposure-related problems.

Contraindication

Tarsorrhaphies are contraindicated in patients with active bacterial infection, though they may be used as an adjunct for treated ulcers with delayed epithelial healing. Extended lateral tarsorrhaphies are relatively contraindicated in patients who are good candidates for procedures

that may offer a better cosmetic result, such as lower lid tightening and lid weight insertion.

Techniques and Principles

Suture tarsorrhaphies can be divided into two categories: those with bolsters and those without. Bolsters are designed to distribute pressure over a larger surface area. They are required when sutures are passed through the skin as well as the lid margin, rather than through the lid margin alone. Popular bolster materials include intravenous tubing, cotton fluff, and foam suture packaging material. The standard technique entails passing both ends of a double-armed silk suture through the first bolster, then through the upper and lower lid skin and tarsal plates, and finally through a second bolster. Tying the two free ends results in complete lid closure. A bow closure allows the tarsorrhaphy to be opened for eye inspection. An alternative method known as the "drawstring temporary tarsorrhaphy" uses a sliding third bolster to open and close the eye (Kitchens et al. 2002). A bolsterless tarsorrhaphy entails taking tarsal bites through the meibomian gland orifices with a single-armed silk suture. The free ends are then tied, apposing the lids (McInnes et al. 2006). This type of tarsorrhaphy is harder to open without cutting.

Lateral tarsorrhaphy entails sharply separating the anterior and posterior lamellae of the eyelids over the desired distance. The posterior lamellae are then sutured together, often after the cutaneous margins have been excised to permit the adhesion of raw tarsal margins.

Outcome

Temporary suture tarsorrhaphy is generally very effective. Cosar and colleagues reported a 91% success rate for the treatment of non-healing epithelial defects (Cosar et al. 2001). Alternatives such as cyanoacrylate glue, tape, and upper eyelid appliques have not been widely adopted because they lack the durability and efficacy of tarsorrhaphy (Ehrenhaus and D'Arienzo 2003; Robinson et al. 2006).

Complications

Bolster suture tarsorrhaphies are prone to cheesewiring if they are frequently and aggressively manipulated or if the tarsal bites are not substantial. Lateral tarsorrhaphies can be divided sharply at a later date, but may result in lid scarring, trichiasis, and a suboptimal cosmetic outcome.

Cross-References

- ▶ Cyanoacrylate Adhesive
- ▶ Epithelial Defects
- ▶ Exposure Keratitis/Keratopathy
- ▶ Lagophthalmos
- ▶ Tarsal Plates/Tarsus
- ▶ Ulcers

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Tarsotomy

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Synonyms

Lateral tarsotomy; Transverse tarsotomy procedure; Wies procedure

Definition

A surgical procedure involving an incision and sometimes excision of the tarsal cartilages.

Indication

Transverse tarsotomy and lid margin rotation is a procedure that is effective in repositioning and everting a lid margin without requiring external incisions or grafting. This procedure may be used to evert the upper or lower eyelids for treatment of trichiasis and involutional and cicatricial entropion. Congenital and acute spastic entropion may spontaneously resolve with medical management and without surgical repair.

Recently, lateral tarsotomy has been used to increase lateral access to the orbit without the need for lateral canthotomy, which can have the major disadvantage of difficulty in resuspension of the lateral canthal tendon, leading to unaesthetic outcomes (Emam et al. 2016).

Contraindication

Contraindications to the tarsotomy procedure are mostly related to general medical condition and preoperative risk to the patient. The procedure may be contraindicated in patients with uncontrolled medical comorbidities, high systemic anticoagulation, or conditions that interfere with appropriate positioning or safe management of the patient during the procedure.

Techniques and Principles

A standard tarsotomy procedure for a lower lid entropion is performed as follows:

1. After skin preparation, infiltrate the entropic lid with local anesthetic consisting of a 50:50 mixture of 2% lidocaine w/epinephrine 1:100,000, 0.75% bupivacaine, and 150 U hyaluronidase.
2. Drape patient in a sterile fashion and place a protective contact lens in the eye being operated on.
3. Retract the lower lid with a 4-0 silk traction suture and make an incision across the inferior tarsal border.
4. Bluntly dissect in the suborbicularis plane down to the inferior orbital rim.
5. If scar tissue is present, e.g., in the case of a cicatricial entropion, dissect the scar tissue off the retractors and elevate the edge of the retractors.
6. Beginning laterally, pass both arms of a 6-0 Vicryl suture anteriorly to posteriorly first through the edge of the retractors and then through the superior edge of the conjunctiva. Then, reverse the needles, enter the inferior tarsal border, and exit through the skin just below the lashes.
7. Place identical sutures centrally and medially across the lid and tie each of the sutures, which rotate the lid margin outward.
8. If horizontal lid laxity is present, a tarsal strip procedure (see "▶ Tarsal Strip Procedure" chapter) may be incorporated during the tarsotomy procedure.

*Tarsotomy for an upper lid entropion would be performed using the steps outlined above but in the anatomical mirror image.

A modified tarsotomy technique may be used to treat *severe* cicatricial entropion. A simple modification involving "two backcuts" at both ends of the transverse tarsotomy allows the distal tarsal fragment to move more freely, which may increase the success rate in cases of severe cicatricial entropion (Chi et al. 2016).

In cases where trichiasis is limited to a small segment of the lid, tarsotomy with lid margin rotation restricted to the affected lid area may be indicated.

Outcome

Transverse tarsotomy produces excellent cosmetic and functional results when used to treat patients with entropions and severe trichiasis.

The tarsotomy procedure has a reported 94% success rate for mild to moderate nontrachomatous cicatricial entropion with trichiasis and a 55% success rate for severe cicatricial entropion with trichiasis (Kersten et al. 1992). The modified tarsotomy outlined above may have a higher success rate in the treatment of severe cicatricial entropion (Chi et al. 2016). A randomized clinical trial comparing bilamellar tarsal rotation (BTR) versus transverse tarsotomy with lid margin rotation (TTR) found that TTR and BTR were successful in 95% and 86% of eyelids with minor trachomatous trichiasis, respectively, and in 84% and 86% of eyelids with major trachomatous trichiasis, respectively. Overall, the TTR group had fewer complications than BTR at 3 months of follow-up (Adamu and Alemayehu 2002). Another study reported an 89% success rate at 6 months for the correction of trichiasis and cicatricial entropion secondary to trachoma (Ali et al. 2012).

Complications

Complications of the tarsotomy procedure include failure of entropion correction or recurrence, and typical surgical risks such as infection, bleeding, and wound dehiscence. Attention to appropriate surgical technique and careful burying of deep sutures aid in the reduction of suture granuloma formation and minimizes complications.

Cross-References

- ▶ Congenital Entropion
- ▶ Melasma, of Eyelids
- ▶ Tarsal Strip Procedure
- ▶ Wies Repair

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Tarsus

▶ Tarsal Plates/Tarsus

TASS

▶ Toxic Anterior Segment Syndrome

Tay-Sachs Disease (GM2 Gangliosidosis Type I)

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Synonyms

Amaurotic familial idiocy; GM2 gangliosidoses; β-Hexosaminidase A deficiency

Definition

Tay-Sachs disease (TSD) is a rare inherited neurodegenerative disorder. It is the most common of

the three variants of a heterogenous group of lysosomal lipid storage disorders known as GM2 gangliosidoses. Each variant refers to a different underlying defect of the enzyme complex required for the GM2 ganglioside catabolism. TSD is characterized by an excessive accumulation of the GM2 ganglioside substrate within neuronal lysosomes and leads to eventual cell death. The main features of the disease are neurological and ocular deterioration. It is classified based on the age of onset:

1. Infantile acute TSD (Type I GM2 gangliosidosis)
2. Juvenile subacute TSD (Type III GM2 gangliosidosis)
3. Late infantile subacute-to-chronic TSD (B1 variant of GM2 gangliosidosis)
4. Adult chronic-type TSD (GM2 gangliosidosis)

Etiology

GM2 ganglioside accumulation in TSD occurs due to specific absence or defect of the alpha subunits of β-hexosaminidase A (Hex A). An autosomal recessive mutation in *Hex A* (15q23-q24), which codes for the Hex A enzyme necessary for GM2 ganglioside degradation, is responsible for disease. This process leads to systemic GM2 ganglioside accumulation primarily in the neurons of the central nervous system and retina leading to neurodegeneration and blindness, respectively (Goldman and Schafer 2012).

Clinical Presentation

The "classic" infantile acute TSD generally manifests by the age of 6 months, but precursor symptoms such as hyperacusis may be present from birth. By the age of 3–6 months, neurological symptoms and signs begin to emerge with the development of hypotonia and evidence of delayed child development. By the age of 1 year, affected patients may be unable to sit, stand, and vocalize, and may develop spasticity and convulsions. They may also develop ataxia, muscle wasting with motor degeneration, and deafness. GM2 ganglioside accumulation of 200 times the normal levels in the brain results in macrocephaly. Death occurs by the age of 3–4 years, usually due to pneumonia.

The most common ocular findings in infantile acute TSD are a macular cherry-red spot and optic atrophy. Histologically, corneal endothelium may be filled with vacuoles; however, corneal clouding has not been reported. It is more likely to occur in closely related Sandhoff disease of similar pathophysiology and aggregation of GM2 ganglioside. Supranuclear neurological involvement of TSD can also manifest as nystagmus and dysconjugate eye movements. The onset of blindness usually occurs later in the first year of life.

The macular cherry-red spot is characteristic hallmark for TSD, which simultaneously presents at 6 months of age with neurological signs and symptoms. This is a result of gangliosidic accumulation within intracytoplasmic membranous bodies of perifoveal retinal ganglion cells. This leads to a deterioration of the inner retinal transparency and causes production of a creamy halo outlying the ganglion cell-free portion of the macula. By the age of 1 year, the cherry-red spot diminishes as a result of retinal ganglion cell death and gliosis along with optic atrophy. Eventual blindness occurs by the age of 18 months as a consequence of optic atrophy and cortical disease.

In contrast to the infantile acute TSD, juvenile- and adult-onset TSD follow a prolonged course with no ethnic predilection. Patients may develop dysarthria and gait disturbances. Other clinical features may include cerebellar atrophy with ataxia, peripheral neuropathy, tonic-clonic or myoclonic seizures in some children, and psychiatric disturbances. It is important to note that vision remains intact with no optic disk atrophy.

Diagnosis

A definitive diagnosis of TSD mainly relies on assaying Hex A enzyme in serum, leukocytes, or cultured skin fibroblasts. A finding of decreased total Hex A is diagnostic for TSD.

An ophthalmic evaluation showing evidence of macular cherry-red spot can also help diagnose

TSD. Diagnosis of infantile acute TSD is usually suspected in an infant with neurological features and a macular cherry-red spot.

Differential Diagnosis

The clinical presentation of TSD is similar to the other two variants of GM2 gangliosidoses: Sandhoff disease and hexosaminidase activator deficiency. These disorders may be clinically indistinguishable in some cases. GM1 gangliosidoses also present with similar signs and symptoms such as hyperacusis at birth. Other metabolic storage diseases should be considered where macular cherry-red spot is a feature such as Niemann-Pick disease.

Prophylaxis

Carrier screening of all couples with at least one member of Ashkenazi Jewish descent is recommended before pregnancy to identify couples at risk. The test targets couples of Ashkenazi Jewish, French Canadian, and Cajun descent due to increased prevalence of TSD carriers in these population subsets. The level of Hex A activity in peripheral leukocytes or plasma is used to establish carrier state in couples. DNA analysis for selected alleles may also be performed.

Additional molecular studies should be conducted in identified carriers to elucidate exact molecular defect. This facilitates more specific identification of carriers within the family and prenatal diagnosis in high-risk couples via enzymatic and genotypic studies.

Prenatal amniocentesis or chorionic villus sampling test for Hexosaminidase A in first trimester of pregnancy serves as an accurate and reliable screening test in carrier-state couples.

Therapy

No treatment currently exists for TSD. Current therapeutic techniques are symptomatic and aimed at managing associated conditions. A multidisciplinary approach involving medical geneticists, neurologists, psychiatrists, and ophthalmologists is essential (Kliegman et al. 2011; Goldman and Schafer 2012; Copeland and Afshari 2013).

Prognosis

Infantile acute TSD is often fatal by the age of 3–4 years. Juvenile TSD is fatal by the age of 10–15 years. Most patients with adult chronic-type TSD have a slightly decreased life expectancy of 50–60 years (Miller et al. 2005; Swaiman et al. 2012).

Epidemiology

The prevalence of TSD is highest among patients with Jewish descent, especially those of Eastern European Ashkenazic origin, who have a carrier frequency of 1 in 25. Populations of French Canadian and Cajun descent are also considered to be high risk.

In the general population, the incidence of TSD has been approximated to be 1 in 112,000 live births. The prevalence of TSD was 1 in 3900 live births among Ashkenazi Jews, but prenatal screening tests for TSD have shown marked reduction in this figure (Miller et al. 2005; Swaiman et al. 2012).

Cross-References

► Mucopolysaccharidosis

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TBUT

▶ Tear Breakup Time

Tear Breakup Time

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Synonyms

Breakup time (BUT); Fluorescein breakup time (FBUT); TBUT

Definition

The tear breakup time is a diagnostic procedure that examines the time that it takes for dry spots to appear on the corneal surface after blinking (Savini et al. 2008).

Purpose

The purpose of the TBUT is to evaluate the stability of the tear film and to detect the presence of evaporative dry eye. A TBUT greater than 10 s is considered normal. A value of less than 5 s indicates significant dry eye disease (Asbell and Lemp 2006).

Principle

The TBUT is performed as follows (Kastelan et al. 2013):

- Fluorescein dye (1–5 μl of 2% sodium fluorescein) is added to the lower fornix of the eye using a pipette or strip.
- The patient is asked to blink a few times in order to distribute the fluorescein and then is instructed to abstain from blinking.
- The tear film is then observed under a slit lamp using a broad beam with a cobalt blue filter.
- The presence of black spots will indicate dry spots on the tear film.
- The tear breakup time is the time it takes after the patient starts to abstain from blinking until the dry spots appear on the corneal surface.
- The patient is then asked to blink freely until repeating the test. The mean of three trials is recorded.

Indication

The TBUT is used to diagnose tear film instability and is part of the diagnostic workup for dry eye disease.

Contraindication

No noted contraindications to perform the TBUT.

Advantage/Disadvantage

Advantages (Savini et al. 2008):

- Widely used
- Commercially available
- Easy to perform
- Less expensive than noninvasive techniques

Disadvantages (Savini et al. 2008):

- Lack of standardized procedure for applying the fluorescein:
  (a) Adding the fluorescein has to be done carefully, in order to avoid reflex tearing. Reflex tearing could artificially lengthen the tear breakup time.

(b) Uncontrolled volumes of fluorescein given could also artificially lengthen the tear breakup time.
- Invasive because it involves using fluorescein in the eye.
- Findings of TBUT often do not correspond to symptom severity.

Cross-References

- ▶ Dry Eye
- ▶ Keratoconjunctivitis Sicca
- ▶ Schirmer Tests

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Tear Deficiency

- ▶ Keratoconjunctivitis: Overview

Tear Film (Tears)

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Definition

A dynamic and complex precorneal gel that protects and supports the ocular surface.

Structure

Traditionally the tear film was described as having three distinct layers – an inner mucin layer, an aqueous layer, and an outer lipid layer. This concept has evolved over the years; the current model of the tear film consists of a mixed inner aqueous-mucins gel with an outermost lipid layer (Pflugfelder et al. 2000; Rolando and Zierhut 2001; Lemp 2008; Peters and Colby 2013).

The aqueous component of the aqueous-mucins gel is mainly produced by the main and accessory lacrimal glands (Rolando and Zierhut 2001).

The mucin portion of the aqueous-mucin gel is comprised of both transmembrane and secretory mucins. Mucins are glycoproteins which have a negative charge; as such they are also highly hydrophilic and able to mix well with the aqueous portion of the tear film. They are more densely distributed closer to the ocular surface. Transmembrane mucins are produced by the corneal and conjunctival epithelial cells and anchored to the ocular surface epithelial cells. These mucins also interact with the overlying secretory mucins in the tear film. Secretory mucins are further subdivided into gel-forming (produced by the conjunctival goblet cells) and soluble (produced by the lacrimal gland) mucins (Lemp 2008; Peters and Colby 2013).

The remaining composition of the aqueous-mucin gel has not been completely determined, but it contains a complex mixture of electrolytes, immunoglobulins, enzymes, antimicrobial proteins, hormones, vitamins, cytokines, and growth factors (Pflugfelder et al. 2000; Rolando and Zierhut 2001; Peters and Colby 2013). The outermost lipid layer is secreted by the Meibomian glands. The portion adjacent to the aqueous-mucin gel consists of hydrophilic polar lipids, while the lipids overlying this base layer are hydrophobic nonpolar lipids. The two layers of lipids contain hydrophobic bonds between them (Pflugfelder et al. 2000; Peters and Colby 2013).

Function

The tear film is critical to the integrity of the ocular surface by performing many roles including:

Allowing nutrients and oxygen to reach the corneal and conjunctival epithelia
Protecting the cornea from mechanical damage from lid forces Lubricating the ocular surface
Preventing adhesion of material (cells, pathogens, debris) to the ocular surface
Defending against infection
Serving as the first encountered refractive surface of the eye (Rolando and Zierhut 2001; Peters and Colby 2013).

Clinical Relevance

Abnormalities in the tear film can increase the risk of infection, cause dry eye and its sequelae, and reduce vision.

Cross-References

- ▶ Accessory Lacrimal Glands
- ▶ Dry Eye
- ▶ Glands of Krause, Glands of Moll, Glands of Wolfring, Glands of Zeis
- ▶ Tear Breakup Time

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Tear Lake

- ▶ Precorneal Tear Film

Tear Meniscus

- ▶ Precorneal Tear Film

Tearing (Epiphora)

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Synonyms

Epiphora

Definition

It is characterized by an abnormal chronic overflow of tears onto the cheeks, generally due to lacrimal drainage impairment or excessive lacrimal production.

Etiology

Tearing is part of the normal eye function; it provides not only a lubricated layer to protect the ocular surface but also is a natural barrier enriched with immunoglobulins and lysosomes to prevent any potential infection (Krachmer et al. 2011).

Many different conditions have been associated to cause epiphora and have been classified into chronic overproduction of tears, outflow obstruction, and failure of the tear pump (Krachmer et al. 2011).

Occurrence

Abnormal tear outflow is often unilateral. Overall, patients complain of ocular discomfort and blurry vision. A wide variety of medical conditions affecting the ocular surface, iatrogenic surgical manipulation of the lacrimal system, and the use of some

medications present with epiphora (Millodot 2009; Krachmer et al. 2011; 2013–2014 Basic and Clinical).

Classification

In general, tear dysfunction can cause chronic ocular irritation, hence epiphora. Disorders in the ocular surface causing irritation present with abnormal tearing including blepharitis; allergic, atopic, and vernal conjunctivitis; superior limbal keratoconjunctivitis; inflamed pterygium; conjunctival neoplasm; and corneal foreign bodies, among others (Krachmer et al. 2011). Furthermore, chronic eye exposure such as malposition of the globe in the case of proptosis secondary to thyroid eye disease, intraorbital neoplasia, or nonspecific chronic inflammation and eyelash and eyelid contour abnormalities or malposition such as epiblepharon, lower lid entropion or ectropion, and trichiasis have also been described as causes of ocular exposure leading to epiphora (Krachmer et al. 2011).

Abnormal tear outflow due to lacrimal system obstruction can also present with epiphora. Punctal stenosis, which is often associated with punctual entropion, can be in some cases severe and results in epiphora (Millodot 2009). Other disorders involving the puncta size like occlusion, stenosis, or secondary enlargement most of the times, after surgical procedures, can also lead to abnormal tearing (Millodot 2009). Several ocular conditions have been associated with punctal stenosis, congenital absence, or any particular defect or dysgenesis of any portion of the lacrimal outflow system. Conjunctivochalasis, enlarged caruncle, chronic ocular surface cicatrizing disease (Stevens-Johnson syndrome or pemphigoid), chronic exposure, and external beam radiation can also lead to punctal stenosis or complete punctum closure leading to epiphora (Millodot 2009; Krachmer et al. 2011).

Obstruction at the canaliculus secondary to trauma, tumor excision, idiopathic scarring, topical ocular medications, and use of chemotherapeutic agents that can lead to secondary sclerosing canaliculitis, such as docetaxel, used as therapy in patients with metastatic breast cancer, can cause canalicular stenosis and secondary obstruction of the tear outflow (Krachmer et al. 2011; 2013–2014 Basic and Clinical).

Lacrimal sac obstruction secondary to neoplasia and other inflammatory conditions including Wegener's granulomatosis and sarcoidosis can also present with chronic abnormal tearing.

Finally, when the lacrimal pump is abnormal or presents some sort of failure like in paralytic ectropion where the stretched or paretic orbicularis muscle fibers on the lower eyelid, particularly, Horner's muscle, are unable to generate enough pressure in order to pump the tears out through the nasolacrimal duct and subsequently, epiphora.

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Tearing, Reflex, Absorption of Ocular Medication

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Definition

Reflex tearing is the stimulated production of tears beyond the normal basal secretion; it may be stimulated by ocular discomfort including irritation from topically applied ocular medication.

Structure

The main lacrimal gland receives both neural and humoral stimulation. It is innervated by parasympathetic, sympathetic, and sensory nerves. Secretion from the lacrimal gland occurs during reflex tearing in response to ocular surface irritation, psychogenic tearing, or aberrant regeneration.

Stimulation of sensory nerves in the cornea or conjunctiva initiates the afferent limb of the tear reflex arc, and the efferent parasympathetic and sympathetic fibers stimulate lacrimal gland secretion.

Tears drain into the nasolacrimal system, and lacrimal outflow is facilitated by the blink mechanism.

The normal human tear volume is approximately 11 μl and the inferior conjunctival cul-de-sac can hold up to approximately 30 μl. Tear volume may expand physiologically during reflex tearing described above or with administration of eye drops. Excess volume spills over the lid margins onto the cheek and the rest exits via the puncti into the nasolacrimal system.

Function

Reflex tearing protects the ocular surface.

Clinical Relevance

The majority of eye medications are administered topically in the form of eye drops. The goal of this mode of drug delivery is to maximize concentrations in the ocular tissue and to minimize systemic absorption which could lead to toxicity.

Reflex tearing adversely affects drug absorption. The inferior cul-de-sac that holds the drug reservoir has a limited volume. Reflex tearing drives overflow onto the skin or into the nasolacrimal system. This decreases the amount of drug delivered and the contact time of the drug with the cornea. Improper instillation of drops as well as the composition of the medication or preservatives may cause ocular irritation resulting in reflex tearing.

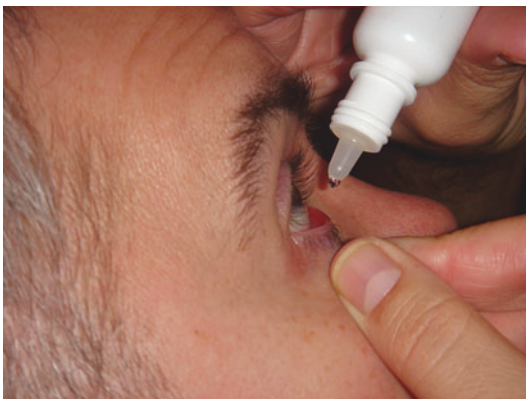
The preferred method of drop instillation is to gently pull the lower lid away from the globe creating a cul-de-sac. A single drop should be placed in the cul-de-sac, and the tip of the bottle should not touch the cornea or eyelashes (Fig. 1).

Blinking also decreases the bioavailability of medication. Each blink promotes drainage of the tear lake into the nasolacrimal system. Absorption of the drug through the highly vascularized nasal mucosa can result in systemic toxicity.

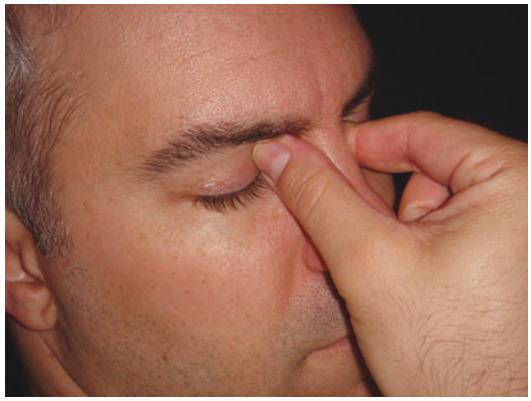
Not blinking but keeping the eyes closed after drop instillation increases bioavailability and decreases systemic absorption. Further benefit is obtained with digital compression over the medial canthus (Fig. 2). Punctal occlusion can reduce by 65% the amount of drug entering the nasolacrimal system.

It is important to educate patients about proper drop instillation and punctual occlusion to limit ocular irritation and reflex tearing and to ensure maximal ocular absorption.

Other methods to improve bioavailability include increasing the frequency of drop instillation and adjusting the lipid solubility, osmolarity, and pH of medications. Use of ointments, sustained-release gels, collagen corneal shields,



Tearing, Reflex, Absorption of Ocular Medication, Fig. 1 Eye drop administration: The head should be tilted back while gently pulling the lower lid away from the globe. The patient should look up to prevent the drop from falling on the cornea, which would stimulate tearing. One drop should be placed in the cul-de-sac taking care that the bottle does not touch the eyelashes or eyelids



Tearing, Reflex, Absorption of Ocular Medication, Fig. 2 Punctal occlusion: Using the thumb and forefinger, the patient applies pressure to the medial canthal region with the lids closed for 2 min

and prodrugs may increase bioavailability. In addition, for some medications and diseases, alternate routes of local administration include intraocular or periocular injections.

Cross-References

- ▶ Accessory Lacrimal Glands
- ▶ Intravitreal Injections
- ▶ Lacrimal Nerve
- ▶ Periocular Injection of Ocular Drugs
- ▶ Tearing (Epiphora)

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Tectonic Graft

▶ Tectonic Penetrating Keratoplasty, for Herpetic Keratitis

Tectonic Penetrating Keratoplasty, for Herpetic Keratitis

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Synonyms

Reconstructive corneal graft; Tectonic graft

Definition

A type of corneal graft intended to restore the integrity of the globe, or normal corneal thickness, such as in diseases-causing corneal thinning and perforation. Untreated or unresponsive HSV keratitis especially in the form of "necrotizing stromal keratitis" may result in stromal melting with subsequent corneal thinning and perforation. Another scenario for corneal perforation secondary to herpetic keratitis is a patient with persistent epithelial defect due to neurotrophic postherpetic keratitis. This latter group of patients has little or no active stromal inflammation. Perforated corneal ulcer needs immediate intervention to protect the ocular integrity and prevent subsequent complications such as endophthalmitis or secondary glaucoma. Small corneal perforation can be managed conservatively with a therapeutic soft contact lenses or adhesive glue. If the perforation is too large for gluing or fails to be sealed satisfactorily after gluing, it may be necessary to repair the perforation site with a full thickness or lamellar tectonic graft. This procedure is defined as tectonic patch graft.

Indication

1. Perforated herpetic corneal ulcer
2. Herpetic corneal ulcer with severe stromal necrosis and corneal thinning impending to perforation
3. Descemetocele formation secondary to necrotizing herpetic keratitis impending to perforation
4. Corneal perforation secondary to persistent epithelial defect with little or no active stromal inflammation (Copeland and Afshari 2013)

Contraindication

Active inflammation and infection before grafting are relative contraindications. All attempts should be made for subsiding any inflammation and infection before surgery, although this may not be possible if the need for grafting is urgent (Copeland and Afshari 2013).

Small corneal perforations especially peripheral ones that could be managed with glue, conjunctival flap or a lamellar patch graft for restoring globe integrity, and then later perform a PKP (Copeland and Afshari 2013).

The surgery should be postponed in children if there are alternative options for restoring globe integrity and also if there is not any risk of amblyopia, in order to avoid complications of pediatric keratoplasty.

Techniques and Principles Outcome

Patients with acute corneal perforations that need tectonic keratoplasty should be admitted to the hospital and not receive any food or drink by mouth until the surgery would be performed.

In suspected situations, gentle B-scan ultrasonography could be performed in order to detect the presence of hemorrhagic choroidal detachments. If present, surgery should be postponed because of the increased risk for expulsive hemorrhage. Also, prompt consultation with a vitreoretinal surgeon should be done.

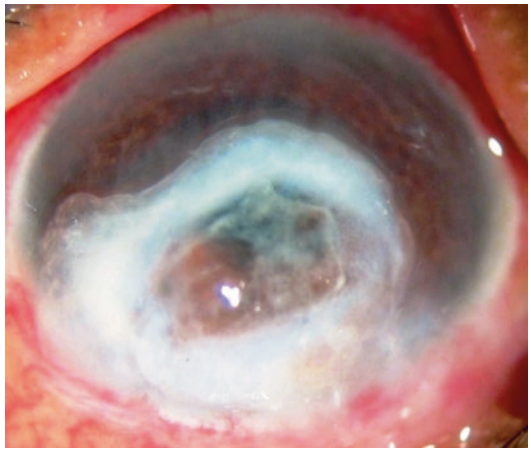
General anesthesia is usually preferred, with the anesthesiologist well aware that the globe is open. An eyelid speculum is then inserted, making sure that there is no external pressure on the globe.

The size of recipient trephination is generally determined by the size and location of the existing corneal perforation. The minimum size of trephine capable of incorporating the entire perforation site and all of infected or ulcerated border is generally chosen. This size could vary between 6.0 and 11.0 mm, with 7.5–8.0 mm being optimal. The donor size is generally considered 0.50 mm more than the recipient trephination size. Viscoelastic could be used for reforming the anterior chamber before trephination and also in maintaining tissue planes.

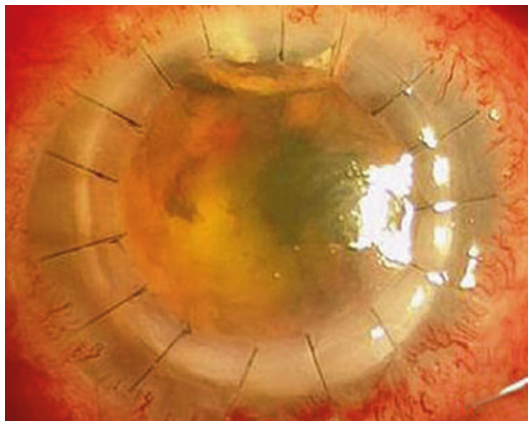
In general, trephination is much more difficult in a perforated eye. The standard handheld trephine without a guard may be preferred. The surgeon should take great care to avoid any external pressure causing protrusion of ocular contents through the perforation site. Alternative option is marking the superficial cornea with the trephine and deepens the mark freehand with a blade. The cornea is entered through the deepened trephination mark.

Another method involves the use of a suction trephine system such as the Hessburg-Barron trephine. In this way, pressure should be exerted outward, avoiding direct pressure on the open globe. Once the trephine is secured on the cornea by suction, trephination is performed by simply rotating the blade of the trephine. Some surgeons have advocated the use of tissue adhesive with or without scleral or corneal patches minutes before trephination to restore the anterior chamber. In this manner, regular trephination could be accomplished in a safer, more effective way (Figs. 1 and 2).

Curved corneal scissors could be used to excise the recipient cornea, with extreme care to avoid cutting the iris or lens. Also, this step is more difficult than usual because corneal opacification and ulcer may hinder the surgeon's view. Once the recipient button is removed, the anterior chamber should be evaluated to detect any peripheral anterior synechiae, posterior synechiae, and cataract. In general, cataract extraction should be postponed because there is an increased risk of



Tectonic Penetrating Keratoplasty, for Herpetic Keratitis, Fig. 1 Perforated corneal ulcer



Tectonic Penetrating Keratoplasty, for Herpetic Keratitis, Fig. 2 Tectonic penetrating keratoplasty

expulsive hemorrhage, vitreous loss, endophthalmitis, and sequestered organisms at the time of the initial procedure. Peripheral anterior synechia and posterior synechiae should be gently lysed, and one or multiple peripheral iridectomies should be performed. Then BSS is used for irrigating the anterior chamber to remove any necrotic or inflammatory debris. A small amount of viscoelastic should be placed in the angle and over the iris and pupil. The donor cornea is then placed over the recipient and secured with at least 16 interrupted 10-0 nylon sutures. Interrupted sutures are preferred due to the tendency of the corneal wound to heal asymmetrically in vascularized or scarred corneas and also the risk of premature suture loosening. The anterior chamber should be reformed with balanced salt solution. The peripheral iris should be swept with the tip of the cannula or cyclodialysis spatula to avoid peripheral anterior synechia formation. Subconjunctival injections of antibiotic and or steroid can be given in the inferior fornix (Krachmer et al. 2011).

Because there is an increased risk of poor epithelial healing after herpetic keratitis, a temporary tarsorrhaphy and/or punctal occlusion are often indicated.

In general, the aim of tectonic keratoplasty is to restore the integrity of globe. Surgery tends to be more successful if the corneal inflammation and infection has been subsided before surgery. Eyes with corneal perforation secondary to persistent neurotrophic herpetic keratitis have better outcomes compared with those of stromal necrotizing keratitis. If the eye still has good visual potential, long-term visual rehabilitation can be attempted later, using anterior segment reconstruction and corneal re-grafting.

Complications

Persistent epithelial defect
Recurrence of herpetic keratitis
Allograft rejection
Secondary graft failure
Glaucoma
Secondary infections
Wound dehiscence (Copeland and Afshari 2013)

Cross-References

- ▶ Corneal Ulcers
- ▶ Necrotizing Stromal Keratitis
- ▶ Primary Endothelial Failure, After Penetrating Keratoplasty

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Teeny's Disease

► Cat Scratch Disease

Telecanthus

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Synonyms

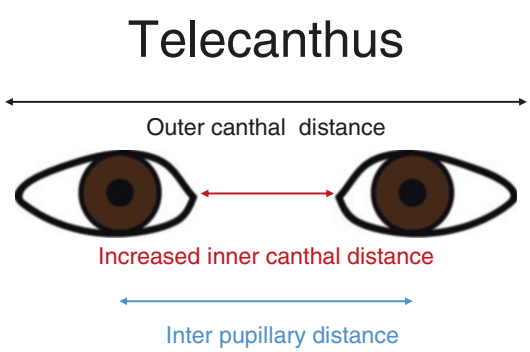
Pseudo-hypertelorism

Definition

Telecanthus derives from tele, which means far, and canthus, which means the corner of the eye. The term was introduced by JC Mustardé in 1963. It describes an increased distance between the medial canthi of the eyes. In primary telecanthus, the interpupillary distance is normal. When the interpupillary distance is greater than normal, it is called secondary telecanthus, which is synonymous with telorbitism. It is important to differentiate telecanthus from telorbitism or orbital hypertelorism, which mean an increased distance between the medial orbital walls.

Structure

Telecanthus is due to displacement of the medial canthi laterally which results in the covering of the medial aspect of the eyes. Unlike hypertelorism, the medial orbital walls are not abnormally separated.



Telecanthus, Fig. 1

Clinical Relevance

Telecanthus may be found in isolation or as part of a syndrome. It makes up part of the syndrome of blepharophimosis as well as many others, including Down syndrome and Ehlers-Danlos syndrome. It can also be due to medial encephaloceles and trauma. It can be treated surgically with medial canthopexy as well as correction of any underlying medial orbital abnormality. In medial canthopexy, generally wires are used transnasally to bring the medial canthal tendons closer together to correct the telecanthus (Fig. 1).

Cross-References

► Telorbitism (Hypertelorism)

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Telorbitism (Hypertelorism)

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Synonyms

Orbital hypertelorism

Definition

Telorbitism, or orbital hypertelorism, is the term used to describe an increased distance between the medial orbital walls. The concept was first described by David Grieg in a lecture in 1924.

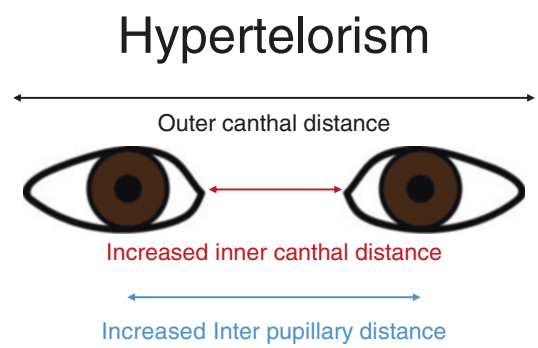
He described an increased interpupillary distance with the term ocular hypertelorism. However, since exophoria can cause an increased interpupillary distance without orbital involvement, the term has been refined to orbital hypertelorism. Orbital hypertelorism refers to an increased medial orbital wall distance. There is no consensus on how to measure telorbitism, and various measurements have been made using interpupillary distance and medial orbital wall distance. The dacryon, which is where the lacrimal, maxillary, and frontal bone meet at the most medial part of the orbit, has also been used to measure this orbital distance. The diagnosis of telorbitism is definitively made radiographically.

Structure

Telorbitism is derived from defects in the face and skull that cause deformation of the orbits laterally. The nasal, frontal, sphenoid, and ethmoid bones may all be involved in this process.

Clinical Relevance

Any condition that causes deformation of the facial bones of the orbit and involves the ethmoid can cause telorbitism. It is found in hundreds of disorders, including in Crouzon, Apert, and Down syndrome. Telorbitism is treated surgically. Several methods of surgical treatment are used and include orbital box osteotomy and facial bipartition surgery. In an orbital box osteotomy excess intervening ethmoid and nasal material are removed. The anterior roof, walls, and floor of the orbit are separated and then are brought together using hardware. Facial bipartition surgery involves resection medially of excess material and also dividing the palate, allowing medial rotation of each superior half of the face which are then connected with hardware (Fig. 1).



Telorbitism (Hypertelorism), Fig. 1

Cross-References

▶ Telecanthus

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Temporal Arteritis

► Arteritic Ischemic Optic Neuropathy

Temporal Artery, Eye Supplied by

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Definition

The temporal artery, specifically the frontal or anterior branch of the superficial temporal artery, anastomoses with several other arteries to supply the eyelid and plays an important role in suitable flap design for orbital surgery.

Structure

The superficial temporal artery arises from the external carotid artery behind the neck of the mandible and passes superficially over the zygomatic process of the temporal bone. The pulse of the superficial temporal artery can be palpated superiorly to the zygomatic arch, just anterior and superior to the tragus of the ear. The mean diameter of the superficial temporal artery at the zygomatic arch is 2.73 ± 0.51 mm (Pinar and Govsa 2006). Approximately 36.9 ± 14.24 mm superior and 17.2 ± 8.2 mm anterior to the posterior-most point of the tragus (Lee et al. 2015), the superficial temporal artery divides into the frontal branch (means size 2.14 ± 0.54 mm), coursing toward the forehead, and the parietal branch (mean size 1.81 ± 0.45 mm), coursing toward the side of the head.

The zygomatico-orbital artery, which can also arise directly from the superficial temporal artery, usually runs parallel to the zygomatic arch to supply the orbicularis oculi. The zygomatico-orbital artery also anastomoses with the transverse facial artery and the frontal branch along its course.

Function

The frontal branch of the superficial temporal artery anastomoses with the supraorbital, superior palpebral, and lacrimal arteries to supply the eyelid. The zygomatico-orbital artery supplies the orbicularis oculi, which is responsible for closing the eye.

Clinical Relevance

The superficial temporal artery is a common site for giant-cell arteritis and therefore is the primary site of biopsy when giant cell arteritis is suspected.

Areas supplied by the superficial temporal artery and its branches may serve as suitable flaps for facial reconstruction. For example, superficial temporal artery island flap combined with auricular cartilage graft may be useful in reconstructions of full-thickness lower eyelid defects. The frontal branch of the superficial temporal artery might be particularly useful in creating local or distant flaps for reconstruction of the forehead or scalp. The zygomatico-orbital artery may serve as a suitable the axial artery of the frontotemporal flap and may also serve as recipient vessel in head and neck reconstruction. However, the zygomatico-orbital artery is absent in 8–9% of patients, which may limit its clinically usefulness.

The frontal branch of the superficial temporal artery may also serve as a landmark for locating the course of the temporal branch of the facial nerve during a facelift. Damage to the temporal branch of the facial nerve causes paralysis of the frontalis, orbicularis oculi, and corrugator muscles, and appropriate identification of this nerve is therefore particularly important. Clinicians

performing botulinum toxin and dermal filler injections should be careful to avoid the frontal branch of the temporal superficial artery to prevent iatrogenic trauma and blood flow obstruction to its supplied tissues.

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Temporal Radiations Lesion

▶ Retrochiasmal Disorders

Temporary Suture Tarsorrhaphy (TST)

▶ Tarsorrhaphy

Tenon's Capsule

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Synonyms

Fascia bulbi

Definition

Tenon's capsule is the fascial sheath within which the eyeball moves; composed of collagen and a few fibroblasts, it fuses posteriorly with the optic nerve sheath and anteriorly with the intermuscular septum.

Tenzel Advancement Flap

▶ Semicircular Flap for Eyelid Repair
▶ Tenzel Flaps

Tenzel Flaps

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Synonyms

Local advancement flap; Semicircular advancement flap; Semicircular flap; Semicircular temporal advancement flap; Tenzel advancement flap

Definition

A tenzel flap is a semicircular local advancement flap, which is often utilized in the reconstruction of full thickness eyelid defects. It allows recruitment of tissues lateral to the lateral canthus to allow medial mobilization of the eyelid and direct wound closure.

Indication

A Tenzel advancement flap is indicated in the reconstruction of moderate upper or lower full

thickness eyelid defects involving approximately 1/3 to 1/2 of the eyelid. The tenzel advancement flap is most commonly employed in eyelid reconstruction following resection of a neoplasm at the eyelid margin or in cases of trauma with full thickness tissue loss.

Contraindications

The defect size and laxity of the individual patient's tissues dictate which reconstructive options are available to the surgeon. Large full thickness eyelid defects, usually greater than 50 % of the eyelid, require reconstructive techniques other than a Tenzel flap to allow recruitment of adequate tissue for reconstruction.

Techniques and Principles

The eyelid defect is assessed and the appropriate reconstructive technique determined. Full thickness eyelid defects encompassing approximately 1/3 to 1/2 of the eyelid, and having intact eyelid structures at the lateral canthus which can be advanced medially, are generally good candidates for reconstruction with a Tenzel flap. A semicircular flap of appropriate size is marked beginning at the lateral canthus. The flap typically extends approximately 1/2 to 2/3 the distance from the lateral canthus to the hairline depending on the extent of advancement required. The flap is created with a superior semicircular incision and rotated inferiorly for lower eyelid defects, or conversely, created with an inferior semicircular incision and rotated superiorly for upper eyelid defects. Lateral canthotomy in combination with cantholysis are performed to free the lateral eyelid and allow mobilization nasally. The wound margins are apposed by direct closure in a standard fashion for full thickness eyelid repair ensuring that excess tension on the wound has been relieved via mobilization of the lateral eyelid segment. Suturing the flap to the orbital rim periosteum can help to form the lateral eyelid contour. The lateral canthus is fixated and the conjunctiva is undermined and advanced to the flap edge if necessary.

Outcome

A semicircuclar incision extending temporally from the lateral canthus with reconstruction of the full thickness eyelid defect is the final result. The lateral most aspect of the reconstructed eyelid will be devoid of eyelashes secondary to the medial advancement of the eyelid tissues formerly residing at the lateral canthal region.

Complications

Excess tension on the newly reconstructed full thickness eyelid defect can result in wound dehiscence. Phimosis and rounding of the lateral canthus can occur with healing particularly if excess wound tension is present. Damage to the zygomatic branch of the facial nerve with resultant orbicularis occuli weakness secondary to deep dissection in the lateral canthal region is possible.

Cross-References

- ▶ Cantholysis
- ▶ Canthotomy
- ▶ Eyelid Reconstruction
- ▶ Lateral Canthal Reconstruction

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Teratoid Cyst

- ▶ Teratomas, Orbital

Teratoid Tumor

- ▶ Teratomas, Orbital

Teratomas, Orbital

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Synonyms

Teratoid cyst; Teratoid tumor

Definition

Orbital teratoma is a rare, congenital choristoma consisting of all three germinal layers in various stages of maturity.

Basic Characteristics

Epidemiology

Orbital teratoma is an uncommon disorder; a report from 1980 cited 51 cases previously documented in the literature. Almost all cases are unilateral; there is a 2:1 female to male preference.

Clinical Presentation

This rare, congenital orbital tumor typically presents with progressive unilateral proptosis in the neonatal period. Massive growth can lead to degenerative changes and distortion of the eye and surrounding bony structures. The walls of the orbit enlarge to accommodate the large mass, and nearby facial structures can exhibit gross deformity. Bony destruction is uncommon. While the eye itself is often structurally normal, proptosis and exposure can lead to keratopathy, erosion, chemosis, and optic atrophy. The enlarging mass can cause stretching and or swelling of the eyelids, and when palpable, the tumor is variably described as fluctuant, cystic, or solid. Glandular epithelial structures with the tumor cysts are responsible for dramatic and rapid growth.

No exposure or environmental risk factor has been identified as causative. Patients typically have normal prenatal and birth history and are otherwise healthy.

Tumors may arise in the orbit and extend secondarily into the cranial cavity or sinuses or present as secondary extension from a large intracranial primary mass.

Etiology

Orbital teratomas are derived from germinal cells. Surface ectoderm is the most prominent germ layer present and gives rise to tumor cystic components, hair follicles, and sweat glands.

Histopathology varies greatly depending on tissue type present in the lesion. Cysts lined by stratified squamous and respiratory epithelium have been reported. Hair follicles, glands, cartilage, teeth, muscle fibers, intestinal material, neural structures, and other tissue types are found within lesions.

Diagnostics

CT and MRI can be used to further evaluate the enlarging orbital mass, though caution should be exercised when using CT scans in young children due to radiation effect. On both CT and MRI, orbital teratomas appear heterogeneous due to the varied tissue components. On CT, the multiloculated mass may contain cysts with fat-fluid levels, solid-enhancing components, and focal calcification secondary to bony elements. While bony orbital enlargement is more common than bone destruction, the mass can extend into adjacent sinuses or intracranial space. Erosion of the sphenoid wing has been reported. On T1-weighted MRI images, fat components and areas of inflammation appear hyperintense to vitreous, whereas on T2-weighted images, fat within cyst walls is hypointense when compared to vitreous and lower water-keratin fluid levels. Solid areas and the rim of the lesion enhance with gadolinium.

Lesions can be biopsied for histopathologic diagnosis prior to resection.

Differential Diagnosis

Suspected in the differential diagnosis should be alternative causes for enlarging orbital mass present at birth. These include rhabdomyosarcoma, retinoblastoma, hemangioma, lymphangioma, plexiform neurofibroma, neuroblastoma, neurofibroma, meningocele, congenital cystic eye, microphthalmos with cyst, congenital glaucoma, and cephalocele.

Therapy

In typical benign lesions, goals of therapy should be to preserve visual function, allow normal orbital-facial development, and optimize aesthetic result. With concern for malignant transformation, the primary concern becomes total tumor resection tumor. When exenteration is warranted, lid-sparing techniques are preferred. If visual function is demonstrated, and the tumor is benign, a conservative approach is pursued. Reports have shown excellent functional and cosmetic results with eye preservation surgery in patients with smaller lesions. Aspiration of the cyst contents may precede complete tumor excision to reduce tumor bulk. Additional craniofacial reconstructive surgery may be necessary following tumor excision.

Prognosis

Orbital teratomas are thought to be benign lesions. Morbidity and mortality increase with tumor invasion of other sites. Teratomas in the head and neck portend a poorer prognosis due to incidence of airway compromise.

Further Reading

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Terrien Marginal Degeneration

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Definition

Terrien marginal degeneration is an uncommon, noninflammatory condition that manifests as slowly progressive bilateral thinning of the peripheral paralimbal cornea.

Etiology

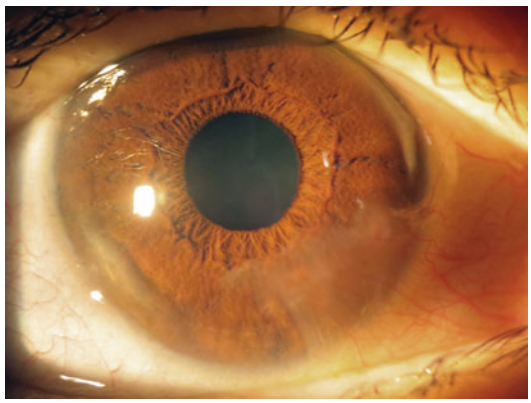
The cause of Terrien marginal degeneration is unknown.

Clinical Presentation

Terrien marginal degeneration classically presents as bilateral peripheral corneal thinning with a

leading edge of lipid. These changes begin superiorly and spread circumferentially. Initially, fine punctate white anterior stromal opacities appear superonasally with a clear space separating them from the limbus. These opacities may later coalesce and extend circumferentially or centrally, and progressive thinning and ectasia may develop. Fine superficial vessels connect these lesions to the limbal arcade. The overlying corneal epithelium remains intact throughout the process. The gutter has a steep central edge and a sloping peripheral edge and becomes wider and more vascularized with time. Lipid deposits form a yellow line central to the advancing edge of the gutter.

Other manifestations of Terrien marginal degeneration have been described. The peripheral ectatic areas can lead to bulging of the cornea and result in breaks in Descemet's membrane. These breaks may lead to the formation of aqueous pockets in the cornea which occasionally connect with the subconjunctival space and result in filtering bleb formation and hypotony. In 20% of patients, pseudopterygia can appear early in the disease state when thinning is minimal. Characteristically, the pseudopterygia occur at either 3 o'clock or 9 o'clock and grow obliquely onto the cornea (Fig. 1). Against-the-rule astigmatism which is characteristic of the disease may also occur, and corneal topography reveals flattening of the peripheral thinned cornea. Although spontaneous perforations are rare, minor trauma to these diseased corneas may result in perforation. An association with other corneal conditions such as posterior polymorphous dystrophy, keratoconus, anterior basement membrane dystrophy, and erythema elevatum diutinum has also been reported.



Terrien Marginal Degeneration, Fig. 1 Terrien marginal degeneration. The classic appearance includes circumferential peripheral thinning with an intact overlying epithelium and a leading edge of lipid. Pseudopterygia can be seen in 20% of patients

Terrien marginal degeneration is a painless condition and the eye classically remains quiet with no evidence of inflammation. However, a rare form of the disease can occur in young individuals with severe pain and recurrent episodes of inflammation, episcleritis, or scleritis. This condition is treated with steroids.

Diagnosis

Terrien marginal degeneration is distinguished from other peripheral corneal thinning diseases by the lack of inflammation, intact epithelium, and slowly progressive course over years. The presence of superficial vascularization and an advancing linear deposition of lipid also aid in the diagnosis. There are no known systemic associations with Terrien marginal degeneration.

Histopathologically, the epithelium is intact with the exception of the basal layer which contains degenerated epithelial basal cells. Bowman layer and the corneal lamellae may be split, fibrillated, fragmented, or absent and replaced with loose vascularized connective tissue. The vessels originating at the limbus migrate centrally within the superficial connective tissue, loop at the central margin of the gutter, and cruise back anteriorly to Descemet's membrane toward the limbus. The lipid line consists of cholesterol crystals deposited anterior to the vascular arcades. Furthermore, histiocytes line the blood vessels and are laden with lipid, collagen and ground substance. The histiocytes demonstrate high levels of lysosomal activity which is evidenced by the continual degradation of corneal tissue. Higher levels of

lysosomal enzymes are present in the tear film of these patients as compared to age-matched controls. Descemet's membrane usually remains intact but may be either thickened or thinned. The endothelium may be normal or attenuated.

Differential Diagnosis

Fuchs superficial marginal keratitis
Marginal furrow degeneration
Arcus senilis
Dellen
Corneal melt associated with collagen vascular diseases
Pellucid marginal degeneration
Sclerokeratitis
Keratoconjunctivitis sicca
Staphylococcal marginal keratitis
Mooren's ulcer
Infectious corneal ulcer

Therapy

Usually no treatment is needed unless perforation occurs or is imminent. Mild astigmatism may be managed with glasses or rigid contact lenses. Surgical correction is indicated for impending perforation of the cornea due to progressive thinning or when severe astigmatism significantly limits the visual acuity. Crescent-shaped lamellar or full-thickness tectonic keratoplasty is most commonly used and has been shown to halt the progression of severe astigmatism for up to 20 years in some cases. Gradual thinning of the grafts may subsequently occur many years later. Annular lamellar keratoplasty grafts may be required in cases of 360° marginal degeneration. Protection with polycarbonate glasses is essential, especially in advanced cases.

Prognosis

Most patients with Terrien marginal degeneration do not progress to corneal perforation and can be managed successfully with glasses or contact lenses. However, approximately 15% of patients present with a perforation and are managed as outlined above. It should be noted that the second eye may be affected decades after the initial eye presents.

Epidemiology

Terrien marginal degeneration is predominant in males, with a 3:1 male to female ratio. It typically occurs in the second or third decade of life.

Cross-References

- ▶ Catarrhal (Marginal Corneal) Infiltrates
- ▶ Corneal Arcus
- ▶ Dellen
- ▶ Fuchs Superficial Marginal Keratitis
- ▶ Keratoconjunctivitis: Overview
- ▶ Keratoconjunctivitis, Sicca: Definition
- ▶ Pellucid Marginal Degeneration
- ▶ Sclerokeratitis

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Terson Syndrome Caused by Subarachnoid Hemorrhage

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Synonyms

Terson's syndrome

Definition

Terson syndrome (TS) is any intraocular hemorrhage associated with subarachnoid hemorrhage and elevated intracranial pressures. It is most commonly associated with subarachnoid hemorrhages caused by ruptured cerebral aneurysms. Originally, TS was defined as vitreous hemorrhage caused by subarachnoid hemorrhage but now includes any intraocular hemorrhage caused by subarachnoid hemorrhage. Intraocular hemorrhage includes the development of retinal, subretinal, preretinal, subhyaloidal, or vitreal blood. The most common presentation for TS is in the subhyaloidal space (Ou and Yoshizumi 2015).

Epidemiology

A review of reports of TS dating back over a 100 years shows that the combination of subarachnoid hemorrhage and vitreous hemorrhage occurred in 13% of hospital admissions. Bilateral vitreous hemorrhage was reported in 56% of those patients. There is no evidence of correlation between gender and vitreous hemorrhage or subarachnoid hemorrhage (Ou and Yoshizumi 2015).

History

A German ophthalmologist, Moritz Litten, first described an intraretinal hemorrhage associated with subarachnoid hemorrhage in 1881 (Litten 1881). However, Albert Terson's description of vitreous hemorrhage following subarachnoid hemorrhage in 1900 is associated with this syndrome (Terson 1900).

Clinical Features

Visual acuities range from 20/20 to light perception in patients where testing is possible. The intraocular hemorrhage is usually superficial to the retina, and in about 56% of patients it occurs bilaterally. Intraretinal and subretinal hemorrhages have been reported. Some preretinal hemorrhages can develop into vitreous hemorrhages within weeks (Medele et al. 1998).

Tests

A reduced red reflex is helpful in evaluating patients who are comatose. Additionally, a B-scan ultrasound can help establish the extent of vitreous hemorrhage. Computed tomography (CT) scan, magnetic resonance imaging (MRI) of the brain, or angiography may be necessary in the evaluation of intracranial hemorrhage (Medele et al. 1998).

Differential Diagnosis

- Subarachnoid hemorrhage especially due to cerebral aneurysm
- Papilledema
- Reduced red reflex

Etiology

TS is commonly caused by subarachnoid hemorrhages due to ruptured cerebral aneurysms. Statistical analysis has not correlated it with a specific aneurysmal location. Other causes include strangulation, trauma, hypertension, tumor, and perioperative and postoperative intracranial bleeding (Ou and Yoshizumi 2015).

Treatment

The intraocular hemorrhage commonly clears spontaneously. Resolution may take months. It may be helpful to elevate the head with bed rest and avoid anticoagulation medication. Nonspontaneous clearing of a large hemorrhage may require a vitrectomy to facilitate clearing. The development of amblyopia is a consideration for early vitrectomy in pediatric cases. It is generally recommended to avoid anticoagulants if possible postoperatively (Ou and Yoshizumi 2015).

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Terson's Syndrome

▶ Terson Syndrome Caused by Subarachnoid Hemorrhage

Tetrapod Fracture

▶ Zygomatic-Maxillary Complex Fractures

Theodore's Superior Limbic Keratoconjunctivitis

▶ Superior Limbic Keratoconjunctivitis

Thermal Cautery

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Synonyms

Diathermy; Electrocautery

Definition

There are many surgical applications of thermal cautery, but this discussion is limited to its use in dry eye disease. This is done by occlusion of one or more puncta using heat. The heat of thermal cautery is generated by a direct or alternating current passing through a resistant metal wire electrode (Hutnik and Probst 1998). This heat is applied to the treatment area, causing localized tissue destruction.

Indication

Dry eye disease
Graft-versus-host syndrome
Intolerance of punctual plugs

Contraindication

Nasolacrimal duct obstruction
Correction with reversible techniques (e.g., punctual plugs) (Ohba et al. 2011)

Techniques and Principles

The lower puncta are typically treated first, with consideration of further treatment of upper puncta if the desired effect has not been fully achieved. Local anesthetic such as 2% lidocaine can be injected in the surrounding skin and conjunctiva, but this is rarely necessary. A sterile, disposable handheld cautery device is used so that the tip is inserted into the punctum. The device is then activated until the punctal tissue becomes white, then saline can be applied to cool the device, and the cautery device is gently removed. No suture is required, and a topical antibiotic is used for several days.

Outcome

Permanent punctal occlusion using thermal cautery has very low recanalization rates (Vrabec et al. 1993; Yaguchi et al. 2012). The goal is improvement in corneal surface with decreased punctate staining as well as symptomatic improvement with less injection, pain, and foreign body sensation.

Complications

The most common complication is epiphora from lack of effective tear drainage. Severe complications are rare and include burns to surrounding tissue, infection, and the inability to reopen the canalicular system if epiphora is bothersome.

Cross-References

- ▶ Dry Eye: Definition
- ▶ Exposure Staining, Keratoconjunctivitis Sicca
- ▶ Graft-Versus-Host Disease: Overview
- ▶ Keratoconjunctivitis, Sicca: Definition
- ▶ Schirmer Tests
- ▶ Tear Breakup Time
- ▶ Tearing (Epiphora)

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Thermal Injury: Overview

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Synonyms

Heat injury

Definition

Thermal injury refers to ocular trauma from radiant energy in the form of heat.

Etiology

Thermal injury is often secondary to trauma such as from hot liquids or gases, explosive materials, or projectiles, and severity varies based on the extent of tissue penetration. In a study of 127 burn patients with ocular involvement at a hospital in the United States, explosions represented the most common etiology, followed by house fires and gasoline (Stern 1996). Iatrogenic burns can also occur during phacoemulsification or with the use of argon laser.

Clinical Presentation

Due to the traumatic etiology of thermal insult, patients may present with multiple ocular injuries, including the eyelid, cornea, and conjunctiva. Eyelids are frequently involved, affecting almost half of the patients examined in the large study referred to above (Stern 1996). Thermal injury to the ocular surface may present with an irregular or missing epithelium; however, a rapid corneal reflex often limits the depth of thermal damage.

In contrast, iatrogenic burns during phacoemulsification may cause significant intraocular injury, as temperature near the phacoemulsification tip may exceed 100 °C (Sugar 1999). Patients with corneal tissue shrinkage near or around the wound may present postoperatively with significant corneal astigmatism or, in severe cases, endothelial failure.

Diagnosis

A thorough history is required to identify etiologic traumatic agents, and penlight examination of the face and eyelids utilized to determine external injuries. Slit-lamp examination is essential to evaluate the distribution and depth of ocular surface burns. Evaluation of the corneal surface with fluorescein to determine the severity of epithelial defects guides therapy and monitors healing.

Differential Diagnosis

Patients with thermal trauma may present with concomitant chemical injury, in which case pH measurement and irrigation of the ocular surface are important.

Prophylaxis

Patients presenting with thermal trauma should be counseled on the use of eye protection and safety precautions to prevent future injuries. Attention to intraoperative fluidics to ensure proper flow of fluid around the phacoemulsification handpiece and evacuation of viscoelastic from the anterior chamber will assist cataract surgeons to minimize thermal trauma to the cornea.

Therapy

Initial treatment of thermal injuries requires immediate evaluation and management of airway and breathing issues, particularly in the setting of facial trauma. Once stable, if chemical exposure is suspected in addition to thermal injury, the eye should be thoroughly irrigated.

Eyelid burns should be covered with ointment, and frequent checks are required to ensure proper coverage of the ocular surface as the eyelid heals, with the use of tarsorrhaphy as needed for severe burns. Frequent lubrication of the cornea with topical antibiotic ointment, such as erythromycin or bacitracin, assists with both infectious prophylaxis and lubrication. Additional lubrication can be provided with artificial tears or gel. In addition, cycloplegics such as atropine or homatropine may assist with comfort.

In advanced thermal corneal burns with limbal stem cell dysfunction, amniotic membrane grafting or conjunctival allograft (if unilateral injury) may assist with epithelial closure, although more data are required to measure the extent of its effectiveness (Clare 2012). Corneal opacity may require corneal transplantation.

Prognosis

Prognosis of thermal trauma depends on rapid intervention and prompt treatment. Eyelid thermal injuries often result in contracture and should be addressed surgically if needed to avoid compromise of the ocular surface, and ocular surface lubrication initiated early to optimize outcomes. In a retrospective review of 66 patients with facial burns, the rate of ocular surgery was reduced by one-third in patients for whom ocular surface lubrication was initiated prophylactically (Spencer 2002), but initial, acute corneal burn with epithelial defect was not associated with a particularly poor prognosis.

Epidemiology

Approximately 16% of ocular burn cases are caused by thermal burns; ocular burns, in turn, represent up to 18% of eye injuries seen in hospital emergency departments.

Cross-References

► Chemical Injury (Burns)

Further Reading

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Thiel-Behnke Dystrophy

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Synonyms

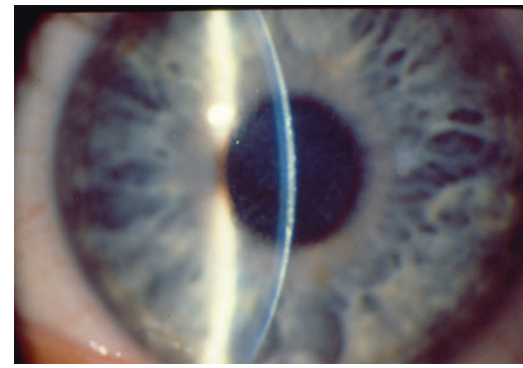
Anterior limiting membrane dystrophy, type II; Corneal dystrophy of Bowman's layer, type II (CDB2); Curly fiber corneal dystrophy; Honeycomb-shaped corneal dystrophy; Waardenburg-Jonkers corneal dystrophy

Definition

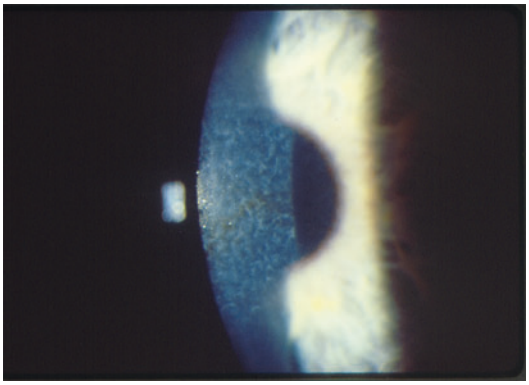
A corneal dystrophy of Bowman's layer characterized by reticular or "honeycomb" opacities and recurrent erosions that lead to ocular pain and visual loss (Figs. 1 and 2).

Etiology

Inheritance is autosomal dominant (Krachmer et al. 2011).



Thiel-Behnke Dystrophy, Fig. 1 Subepithelial "honeycomb" opacities similar to Reis-Bücklers



Thiel-Behnke Dystrophy, Fig. 2 Magnification of subepithelial "honeycomb" opacities

Clinical Presentation

Patients are born with normal corneas and begin to develop signs and symptoms during the first and second decade of life. Symmetrical subepithelial honeycomb-like opacities appear in the central cornea with the peripheral cornea uninvolved. Patients suffer from pain and redness from recurrent erosions and their vision gradually deteriorates (Weiss et al. 2008). The condition is very similar to Reis-Bücklers dystrophy disease, and distinguishing between the two by clinical examination is difficult.

Diagnosis

Differentiation between Thiel-Behnke dystrophy and Reis-Bücklers dystrophy is best made through light and electron microscopy. In Thiel-Behnke dystrophy, light microscopy demonstrates the replacement of Bowman's layer by a fibrocellular layer that has a unique wavy "saw-toothed" pattern. Electron microscopy reveals pathognomonic curly fibers in the region of Bowman's membrane (Krachmer et al. 2011). Confocal microscopy also contributes to the diagnosis by identifying reflective irregular deposits in Bowman's layer and deposits in the basal epithelium with dark edges and homogenous reflectivity (Weiss et al. 2008).

Differential Diagnosis

Differential diagnosis includes Reis-Bücklers dystrophy disease, map-dot-fingerprint dystrophy disease, recurrent corneal erosion disease, macular corneal dystrophy, Fuchs' dystrophy disease, and herpes simplex.

Prophylaxis

No prophylaxis is known; however, topical lubricants are used to prevent corneal erosions.

Therapy

Treatment is initially focused on recurrent erosions. Topical lubrications, contact lenses, and patching are used during this time. Eventually, as corneal scarring develops, superficial keratectomy or phototherapeutic keratectomy (PTK) may be performed. A keratoplasty, lamellar or penetrating, is reserved for when the scarring becomes severe and deep. The dystrophy frequently recurs in the graft (Krachmer et al. 2011).

Prognosis

Progression may be less aggressive than with Reis-Bücklers dystrophy. Recurrent erosions lessen with time. Vision slowly progressively deteriorates until surgical treatment is necessary (Weiss et al. 2008).

Epidemiology

The condition is rare and prevalence unknown.

Cross-References

- ▶ Fuchs' Dystrophy Disease
- ▶ Herpes Simplex Virus
- ▶ Macular Corneal Dystrophy (MCD)

- ▶ Map-Dot-Fingerprint Dystrophy (Epithelial/Anterior Membrane Dystrophy)
- ▶ Recurrent Corneal Erosion
- ▶ Reis-Bücklers Dystrophy

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Third Nerve Palsy

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Synonyms

CN III palsy; Oculomotor nerve palsy

Definition

All of the cranial nerves (CN) controlling extraocular muscle function (CN III, IV, VI) arise from separate nuclei located within the brain stem. The dorsal midbrain contains the nuclei and fascicles for CN III at the level of the superior colliculus. A lesion of CN III can affect all or only a portion of the nerve (i.e., complete or partial CN III palsy). A complete CN III palsy would thus be expected to produce an ipsilateral dilated pupil (internal ophthalmoplegia), ptosis, and an external ophthalmoplegia involving all of the extraocular muscles innervated by CN III (i.e., superior rectus, inferior rectus, inferior oblique, and medial rectus muscles). Thus, the ocular deviation is usually ipsilateral exotropia and hypotropia (i.e., "down and out" position) due to unopposed action of the remaining functioning extraocular muscles (lateral rectus and superior oblique muscles). Affected patients however may not always complain of diplopia due to ptosis which can act as an occluder of the affected eye.

The anatomic course of the third nerve begins at the nucleus, located within the dorsal midbrain. A lesion at this level might produce a "nuclear" CN III palsy. The nuclear innervation to the levator muscle in the upper eyelid is controlled by a single, central caudal subnucleus, and thus, nuclear third lesions produce either no ptosis or bilateral ptosis. In addition, the superior rectus muscle is innervated by the contralateral subnucleus, and thus, a unilateral CN III palsy presenting with a contralateral superior rectus palsy is an obligatory sign of a nuclear CN III palsy unless there are multiple lesions involved.

From the nucleus, the third nerve fibers course together to form the fascicle within the midbrain parenchyma. The nerve then exits the midbrain ventrally and travels anteriorly toward the cavernous sinus in the lateral dural wall, through the superior orbital fissure to the orbital apex, and finally to the CN III innervated extraocular muscles. The third nerve closely follows the path of the posterior communicating artery in the subarachnoid space and in this location is vulnerable to aneurismal compression. The third nerve also carries the parasympathetic pupillary fibers to the iris sphincter from the Edinger-Westphal nucleus in the dorsal midbrain. These fibers are located very superficially in the third nerve as it courses in

close proximity to the posterior communicating artery; thus, an aneurysm of the posterior communicating artery often produces a pupil-involving CN III palsy. The third nerve also contains the somatic ocular motor fibers that innervate the inferior oblique, medial rectus, superior rectus, inferior rectus, and levator palpebrae superioris muscles.

Etiology

Microvascular ischemia is a common underlying etiology of an isolated CN III palsy in adults and represents up to 17–35% of cases in large retrospective pooled series of third nerve palsies (Rucker 2012). Compressive lesions (e.g., aneurysm and neoplasm), however, are responsible for up to 19% of cases (Rucker 2012). A pupil-involved CN III palsy is a red flag for an underlying aneurysm, most commonly at the posterior communicating artery-internal carotid artery junction (34–61% of cases), but basilar tip aneurysms or intracavernous internal carotid artery aneurysms can also produce a CN III palsy (Rucker 2012).

Although meningioma and other benign cavernous sinus lesions can produce a CN III palsy, other more malignant neoplastic causes such as lymphoma or metastases should also be suspected in patients with acute presentations especially in patients with a previous cancer or lymphoma diagnosis. ► Myasthenia gravis should also be considered in any painless, pupil-spared ophthalmoplegia including what might appear to be a pupil-spared CN III palsy. Pituitary adenomas with cavernous extension, other less common neoplastic etiologies (e.g., third nerve schwannoma, intracavernous hemangioma/hemangiopericytoma), and vascular lesions (e.g., intracavernous aneurysm, carotid cavernous fistula) may also occur. Giant cell arteritis should also be considered in the differential diagnosis of new diplopia, including CN III palsy, in elderly patients, especially those with typical symptoms of headache, jaw pain, or concomitant visual loss. Trauma is an uncommon cause, but can also result in a CN III palsy, although this comprises less than 1% of cases in pooled retrospective series (Rucker 2012).

Clinical Presentation

A complete loss of third nerve function results in unopposed action of the lateral rectus muscle (innervated by the sixth cranial nerve) and the superior oblique muscle (innervated by the fourth cranial nerve). This results in the classic presentation in a CN III palsy of an eye that is "down and out" (i.e., the affected eye is abducted and depressed in primary position). Additionally, partial or complete ptosis may be present. A poorly reactive or nonreactive, dilated pupil can also result from loss of parasympathetic iris sphincter innervation. This produces anisocoria that is greater in the light due to the affected pupil's inability to constrict properly. The lid, pupil, or extraocular muscle function can be variably involved or spared in partial third nerve palsies.

As noted above, ipsilateral compression by a posterior communicating artery aneurysm typically involves the pupil because the superficial pupillary fibers are the first to be compromised by an adjacent compressive lesion. In contrast, diabetic (and other small vessel ischemic etiologic) third nerve palsies often spare the pupil, as ischemia affects the deeper penetrating vasa nervorum vessels to a greater extent than the superficial pupillary fibers. Some diabetic ischemic third nerve palsies, however, can involve the pupil, albeit typically with less anisocoria (<1 mm).

Although the "rule of the pupil" states that a pupil-involving CN III palsy is a posterior communicating artery aneurysm until proven otherwise, the absence of pupil involvement does not rule out an aneurysm, as up to 33% of all posterior communicating artery aneurysms do not have pupillary involvement on presentation (Rucker 2012). In some cases, the pupil is not involved because only a portion of the third cranial nerve is affected (e.g., partial palsy or superior division only); thus, the "rule of the pupil" should not be extrapolated to clinically define "pupil sparing" in a partial palsy of CN III.

Diagnostics

Although somewhat controversial, a complete, isolated, acute, painless, CN III palsy in a vasculopathic patient without pupillary involvement could be observed for improvement, as microvascular ischemia is the most likely culprit. Some authors, however, recommend neuroimaging for all CN III regardless of ischemic risk factors. In contrast, if the CN III palsy presents with a "blown" (dilated) pupil, the pretest likelihood for aneurysm is high. In most centers, the best initial imaging study for any patient in an acute, emergent setting, especially in patients with severe pain (e.g., "worst headache of my life"), or altered mental status, is computed tomography (CT) of the brain (non-contrast) to first evaluate for subarachnoid hemorrhage followed with contrast CT angiography (CTA) of the brain. The two CT studies can be combined at most institutions. Unfortunately, CT/CTA is not sufficient to exclude nonvascular causes of CN III palsy, and magnetic resonance imaging (MRI) of the brain and orbits with and without contrast and fat suppression as well as magnetic resonance angiography (MRA) might still be necessary in unexplained CN III palsy. Although CTA is believed to be superior to MRA at most centers, variability in technique, availability of neuroradiologic expertise, variability in interpretation, and sometimes the intrinsic imaging characteristics of the aneurysm itself (e.g., thrombosis, partial flow) can make one technique better than the other in any one individual patient. Specific, customized, individualized discussion and review of the neuroimaging studies with the neuroradiologist is recommended. Standard catheter contrast angiography (CA) should be considered even if the MRI/CT and MRA/CTA combination is negative for aneurysm if there is still sufficiently high pretest suspicion (e.g., painful, pupil-involved CN III palsy) or if the posttest (CTA/MRA) likelihood of aneurysm remains high or uncertain (e.g., CTA or MRA had artifact obscuring a complete 3D rotational view of the posterior communicating artery) (Lee et al. 2009).

Although both MRA and CTA have a sensitivity of close to 98% for the detection of an aneurysm producing a CN III palsy, structural MRI with contrast can better detect nonvascular causes of CN III palsy (e.g., tumor, meningeal disease). Complete CN III palsy with partial pupil involvement (e.g., a larger but reactive pupil or a postsurgical pupil) or partial CN III palsy without pupillary involvement typically requires an imaging study (e.g., CT/CTA then MRI/MRA). However, CA may not be necessary in such cases if the index of suspicion is not as high for aneurysm after adequate non-catheter cranial and cerebrovascular imaging (Lee et al. 2009).

MRI without contrast alone is not recommended because enhancing lesions of the third cranial nerve, meningeal disease, and some tumors (e.g., meningioma) might be missed without gadolinium contrast. Some patients, however, have contraindications (e.g., renal failure or contrast allergy) that may preclude contrast administration. MRA (as opposed to contrast CTA) can be performed with or without contrast. Thus, a non-contrast MRA could be a reasonable second choice to CTA if needed in selected cases especially with MRI contrast contraindications.

Although many authors believe that initial observation for resolution without initial neuroimaging is reasonable for an acute, isolated, painless, pupil-spared CN III palsy in a vasculopathic patient, pain, progression, lack of improvement, or development of aberrant regeneration or any new signs or symptoms during the observation period (i.e., first few weeks to months) should prompt consideration for neuroimaging. On the other hand, MRI/MRA with and without contrast of the head would not be unreasonable even in cases of acute, isolated, painless, pupil-spared, and presumed vasculopathic CN III palsy because some of these patients can harbor an underlying etiology. However, the decision to image in this setting remains controversial because most of these cases will eventually come to imaging because of lack of spontaneous improvement.

Differential Diagnosis

1. Ischemic
2. Aneurysm (posterior communicating artery, intracavernous carotid artery, basilar artery)
3. Orbital apex lesion
4. Uncal herniation (secondary to increased intracranial pressure)
5. Neoplasm (schwannoma, meningioma, pituitary apoplexy)
6. Giant cell arteritis
7. Myasthenia gravis (painless, pupil spared)
8. Ophthalmoplegic migraine (rare)
    1. *Ischemic CN III palsy*: An acute, unilateral, painless, pupil-spared, CN III palsy is most often caused by microvascular ischemia in adults. Typically, there is no pupillary involvement as ischemia involves the deeper penetrating vasa nervorum vessels and not the superficial pupillary fibers. Some diabetic ischemic third nerve palsies, however, do involve the pupil, albeit with mild anisocoria (<1 mm). Most cases of ischemic CN III palsy resolve spontaneously and do not require treatment, with up to 80% resolving in 3 months (Akagi et al. 2008).
    2. *Aneurysm*: The most common location of an aneurysm producing a CN III palsy is the posterior communicating artery-internal carotid artery junction (34–61% of cases), but basilar tip aneurysms can also produce a unilateral or bilateral CN III palsy (Rucker 2012). Ipsilateral compression by a posterior communicating artery aneurysm typically produces pupil involvement. The lack of pupillary involvement in a partial CN III palsy, however, does not obviate the need to rule out a posterior communicating artery aneurysm, as up to 33% of all posterior communicating artery aneurysms do not have pupillary involvement on presentation. Typically, the best initial imaging studies are brain CT/CTA, but MRI/MRA with and without contrast might still be necessary to exclude other non-aneurysmal causes of CN III palsy. However, catheter angiogram still remains the gold standard for excluding aneurysm.
    3. *Orbital apex lesion*: Please see the section on "► Orbital Apex Syndrome" for a more detailed explanation of this disorder.
    4. *Uncal herniation*: The third nerve may be involved in uncal herniation from an expanding mass lesion in which the uncus, located in the medial portion of the temporal lobe, herniates through the foramen magnum, directly compressing the third cranial nerve at the tentorium and causing a CN III palsy. The dilated and poorly reactive pupil associated with uncal herniation is sometimes known as a "Hutchinson pupil."
    5. *Neoplasm (schwannoma, meningioma, pituitary apoplexy)*: Pituitary apoplexy results from acute hemorrhage or necrosis occurring within a preexisting pituitary adenoma. This can cause rapid enlargement of the pituitary gland and compression of the surrounding structures. The most common structures involved by apoplexy are the cavernous sinus (which may result in an acute CN III palsy – see the section on "► Cavernous Sinus Syndrome") and the optic nerves or chiasm, resulting in loss of vision unilaterally or bilaterally.
    6. *Giant cell arteritis (GCA)*: Although GCA typically presents with unilateral or bilateral visual loss (often with pallid optic disc edema), third nerve palsies associated with GCA have rarely been reported. Please see the section on "► Arteritic Ischemic Optic Neuropathy" for more details on this disorder.
    7. *Myasthenia gravis*: The possibility of neuromuscular disease, such as myasthenia gravis, should also be considered in any painless, pupil-spared, ophthalmoplegia which can include the extraocular muscles involved in a typical CN III palsy. Myasthenia gravis is a disease of the neuromuscular junction and can produce any pattern of pupil-spared, non-proptotic ophthalmoplegia and can mimic a CN III palsy. Please

see the section on "▶ Myasthenia Gravis" for more details on this disorder.

8. *Ophthalmoplegic migraine*: Migraine is always a diagnosis of exclusion and is characterized by recurrent episodes of a CN III palsy (or rarely other ocular motor cranial nerve palsies) in a younger patient with a known history of migraines. Because ophthalmoplegic migraine is rare and a diagnosis of exclusion, typically brain and orbit MRI with and without contrast with MRA are necessary to exclude other etiologies.

Prophylaxis

Not applicable.

Therapy

Patching of the affected eye and the use of temporary Fresnel prisms are first-line treatments for an acute cranial third nerve palsy, as they are both noninvasive and reversible. Surgical treatment should be considered only after the diagnostic evaluation is completed. If the deviation fails to improve and fails conservative or prismatic therapy, and the orthoptic measurements have remained stable for at least several months, then strabismus surgery could be considered.

Surgical correction of CN III palsy-related ptosis and strabismus is notoriously difficult. The precise surgical procedures selected depend on the exact pattern of strabismus. Some strabismic procedures commonly employed to alleviate symptomatic diplopia include transposition of the superior oblique tendon, medial rectus resection, and lateral rectus recession (Yonghong et al. 2008). The efficacy of botulinum toxin injection in the treatment of an acute CN III palsy is controversial, but is believed by some to allow medial rectus recovery by relaxing the lateral rectus muscle. Botulinum toxin can also be effective in temporarily treating symptomatic diplopia if the patient is not ready to proceed with more permanent surgical procedures.

Prognosis

Almost half of all idiopathic CN III palsy resolve partially or completely (Rucker 2012). A presumed vasculopathic cranial third nerve palsy has a high rate of spontaneous resolution, with up to 80% resolving in 3 months (Akagi et al. 2008). As a result, in contrast to long-standing deviations that might produce an anomalous head or face position, ischemic CN III palsy typically does not typically result in painful torticollis.

Multiple simultaneous or rapidly sequential cranial neuropathies are atypical and should prompt further evaluation for additional diagnoses with neuroimaging (i.e., "a diabetic patient is allowed only one ocular motor cranial neuropathy at a time"). Aberrant regeneration is essentially never seen after ischemic CN III palsy, and thus if aberrant regeneration is present, this should prompt neuroimaging, including evaluation for neoplasm (especially cavernous sinus) or aneurysm.

Epidemiology

Third nerve palsies represent up to 30% of all cranial nerve palsies in adults (Rucker 2012).

Cross-References

- ▶ Aneurysms
- ▶ Giant Cell Arteritis
- ▶ Myasthenia Gravis, Overview
- ▶ Ophthalmic Migraine
- ▶ Orbital Apex Syndrome in Neuro-Ophthalmology
- ▶ Posterior Ischemic Optic Neuropathy

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Thorazine Retinopathy

► Chlorpromazine, Retinal Degeneration

Thorazine-Induced Retinal Degeneration

► Chlorpromazine, Retinal Degeneration

Three-Dimensional Computed Tomography, in Orbital Evaluation

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Synonyms

Three-dimensional computer tomography volume rendering

Definition

Three-dimensional (3D) computed tomography (CT) combines advances in spiral CT with computer hardware, software, and display technology to create 3D renderings of anatomical structures.

Purpose

3D CT is a useful imaging modality in the evaluation of orbital disease and in preoperative planning for orbital procedures.

Principle

3D CT relies on the same basic physical principles as a spiral CT, which includes the use of x-ray emissions in a cone-beam or fan-beam pattern with a detector to generate cross-sectional images of the body that can be reconstructed in any given plane. Using the conventional fan-beam CT device, the patient is placed horizontally and slowly passed through a circular metal frame that contains an x-ray source and detector. Images are taken as "snapshots" that are aggregated and reconstructed to provide a continuous set of images. Cone-beam CT is particularly useful for craniofacial anatomy and allows for better resolution with lesser radiation compared to the conventional fan-beam CT devices.

In addition to a basic spiral CT, 3D CT relies on computer algorithms to convey 2D images as 3D renderings. The fundamental principle is to carefully compare multiple 2D images to best represent their internal spatial relationship to provide a 3D image. A classic example is a 3D cube, which when imaged using CT shows up as multiple 2D images in various cross sections. 3D rendering techniques, such as, shaded surface display (SSD) and maximum intensity projection (MIP), rely on mathematical formulas that compare these 2D images to display certain image features over others to best represent the 3D spatial relationship. Each 3D rendering technique differs in how the image features are selected, weighed, and projected, which leads to slight variations in the 3D images (Calhoun et al. 1999).

Indication

Orbital trauma, orbital fractures, orbital tumors, orbital infections, thyroid eye disease, proptosis, globe malposition, and preoperative planning.

Contraindication

3D CT has no contraindications separate from a CT in general. These include patients with iodine or contrast allergies, patients with significant renal disease, and pregnant patients.

Advantages/Disadvantages

A spiral CT allows for rapid evaluation and is therefore the preferred modality in emergent situations. 3D CT may add additional clinically relevant data during emergent cases, such as clear visualization of the fracture line and bony displacement of the orbit. 3D CT allows for exquisite visualization of orbital anatomy and is therefore particularly useful in preoperative planning (Sinanoglu et al. 2016).

Metallic objects, such as dental fillings, lead to image artifacts on CT that may obscure key structures. Since CT is classically best for bone assessment, it has limited utility in detailing orbital soft tissue and the orbital apex as compared to MRI. Radiation exposure is another disadvantage, but this can be reduced by 15 times when using cone-beam CT compared to fan-beam CT for orbital assessment (Karatas and Toy 2014). Cost of obtaining a CT machine and the necessary software for 3D rendering may not be feasible for all centers. Lastly, each 3D rendering technique uses slightly different algorithms that may cause variations in 3D images.

Cross-References

► Spiral Computed Tomography, in Orbital Evaluation

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Three-Dimensional Computer Tomography Volume Rendering

► Three-Dimensional Computed Tomography, in Orbital Evaluation

Thrombophlebitis, of Orbital Vein

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Synonyms

Septic thrombosis of orbital veins; Superior ophthalmic vein thrombophlebitis

Definition

Orbital vein thrombophlebitis is a complication of orbital or periorbital infection in which venous drainage is blocked by infectious elements. Most commonly, thrombophlebitis is caused by bacterial infection, but fungi, mycobacteria, and

parasites may also cause venous occlusion. Orbital vein thrombophlebitis may be a sign of concurrent or impending cavernous sinus thrombosis, a serious and potentially deadly infection.

Etiology

Orbital vein thrombosis may result as a consequence of any orbital or periorbital infection. Orbital thrombophlebitis has been reported in the setting of facial cellulitis, orbital cellulitis, dacryocystitis, sinusitis, odontogenic infections, and in Lemierre's syndrome (internal jugular vein thrombophlebitis) (Sanchez et al. 1997; Walker et al. 2002; Schmitt et al. 2005).

Orbital vein thrombosis is a severe and potentially life-threatening complication of orbital cellulitis – because the orbital veins lack valves – infectious thrombophlebitis may track posteriorly into the cavernous sinus.

The zygomyses are feared and potentially life-threatening cause of orbital vein thrombophlebitis. Fungal infections, such as mucormycosis, are angioinvasive and often involve the orbital veins and cavernous sinus.

Clinical Presentation

The orbital veins are valveless and communicate directly with the cavernous sinus, allowing infections to travel directly to the cavernous sinus. A unilateral orbital cellulitis that becomes bilateral is highly suggestive of a cavernous sinus thrombosis arising from septic orbital vein thrombosis (Black and Smith 2012).

Examination findings in the setting of orbital vein thrombophlebitis may include signs and symptoms of orbital cellulitis, such as pain, proptosis, limited extraocular movements, chemosis, ptosis, and optic neuropathy in severe cases. Exam may also reveal dilation of periocular and scleral vessels and periphlebitis or dilatation and engorgement of retinal veins on fundoscopic examination. Cavernous sinus thrombosis may develop as a result of orbital vein thrombophlebitis, and patients may present with high fever, leukocytosis, headache, vision loss, ophthalmoplegia, meningeal signs, and bilateral orbital involvement. Neurologic deficits signify intracranial life-threatening intracranial involvement and may include altered mental status, seizure or focal neurologic deficits (Black and Smith 2012).

Diagnosis

Blood cultures are essential in suspected thrombophlebitis. Positive cultures identify a causative organism and allow for targeted antimicrobial therapy. Any discharge may also be cultured for a causative organism.

Imaging Findings

On CT imaging, the involved orbital vein appears thickened and has nondistinct borders. Contrast-enhanced CT angiography, MR angiography, and MR venography may all demonstrate proximal dilation and distal flow of the affected orbital vein. Imaging may demonstrate a low-density signal within the vein, representing the thrombus. Imaging may also demonstrate signs of associated infection such as proptosis, orbital fat stranding, abscess, or adjacent sinusitis.

In orbital mucormycosis, MRI may demonstrate diffuse orbital findings including proptosis, diffuse abnormal enhancement of the orbital fat, and dilation of the superior ophthalmic veins (Black and Smith 2012).

Differential Diagnosis

The differential for orbital vein thrombophlebitis includes infectious orbital cellulitis (bacterial, fungal, mycobacterial, parasitic, viral), non-infectious orbital inflammation (idiopathic orbital inflammation, sarcoidosis, thyroid eye disease, scleritis, granulomatosis, and polyangiitis), neoplasms, and vascular lesions (carotid-cavernous

fistula, lymphangioma, cavernous sinus thrombosis) (Black and Smith 2012).

Prophylaxis

Appropriate, timely treatment of periocular and orbital infections may prevent these infections from spreading through the orbital veins and causing orbital vein or cavernous sinus thrombophlebitis.

Therapy

Intravenous antibiotic therapy is required for orbital vein thrombosis. Empiric therapy should provide broad coverage for gram-positive organisms, including MRSA, as these bacteria represent the most common causes of orbital cellulitis and orbital infections. Anaerobic and gram-negative organisms have also been implicated. Initial therapy typically includes a third- or fourth-generation cephalosporin, metronidazole, and a penicillinase-resistant penicillin. Vancomycin may be started in patients with penicillin allergy and in suspected MRSA infections. Empiric antimicrobial therapy may also include antifungals where indicated, such as in immunosuppressed patients and poorly controlled diabetics, where fungal disease is suspected (Black and Smith 2012).

The role of anticoagulation remains controversial. Anticoagulation has been proposed as an adjunctive therapy in order to prevent extension of thrombophlebitis and to increase antibiotic penetration. Given the risk of intracranial and systemic hemorrhage, anticoagulation should be instituted with caution, and patients should be monitored carefully.

Prognosis

Orbital vein thrombosis represents a serious complication of orbital or periorbital cellulitis and may be fatal. In the classification system of orbital cellulitis proposed by Chandler in 1970, cavernous sinus thrombosis is classified as group V – the most severe classification (Black and Smith 2012).

Epidemiology

Orbital vein thrombophlebitis is a rare complication of orbital or periorbital infections.

Cross-References

▶ Cavernous Sinus Syndrome
▶ Orbital Cellulitis

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Thygeson's Superficial Punctate Keratitis

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Synonyms

Thygeson's superficial punctate keratopathy

Definition

Thygeson's superficial punctate keratitis (TSPK) is an uncommon, chronic, bilateral epithelial keratitis characterized by coarse, elevated, and discrete corneal epithelial lesions.

Etiology

The etiology of Thygeson's superficial punctate keratitis is unclear. Some experts have hypothesized a viral etiology due to its resemblance to other viral keratitis. No studies have proved the relationship between TSPK and a virus using cultures or PCR.

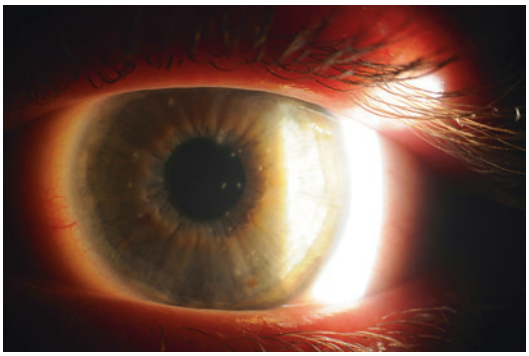
TSPK has been postulated to be an immune-mediated disease. Its response to topical steroid therapy supports the idea of a possible inflammatory etiology. Studies have shown an association between HLA-DR3, HLA-DW3, and TSP-K. These antigens have been described in inflammatory conditions (i.e., Graves' disease and IDDM). No studies have shown a direct relationship between systemic inflammatory conditions and Thygeson's superficial punctate keratopathy.

Allergy has also been postulated as a possible etiology, although no signs of ocular allergic disease are seen during exacerbations.

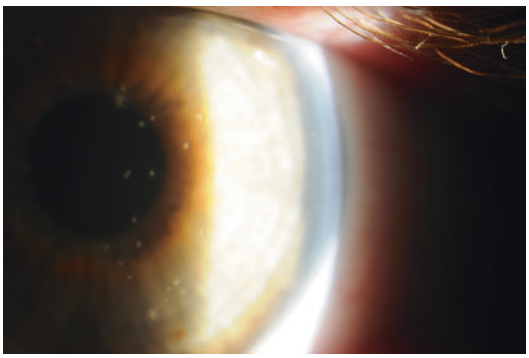
Clinical Presentation

Patients with TSPK present with symptoms of photophobia, foreign body sensation, pain, and tearing. The conjunctiva is usually quiet or mildly injected. The disease is usually chronic and recurrent.

Symptoms are usually worse than the clinical findings. Slit lamp examination shows numerous, discrete, fine, oval opacities located in corneal epithelium (Figs. 1 and 2). Lesions are usually located in the central cornea, averaging 15–20 per eye. They stain with fluorescein and rose bengal during exacerbations. Mild epithelial and subepithelial edema may be seen.



Thygeson's Superficial Punctate Keratitis, Fig. 1 Thygeson's superficial punctate keratopathy



Thygeson's Superficial Punctate Keratitis, Fig. 2 Thygeson's superficial punctate keratopathy, higher magnification

Exacerbations are self-limited but they can take 1–2 months to resolve. Between attacks, cornea may show no abnormalities or mild subepithelial scars.

Diagnosis

Diagnosis is made clinically.

Differential Diagnosis

Differential diagnosis includes viral keratitis (herpes simplex, varicella zoster, adenovirus), dry eye syndrome, keratoconjunctivitis sicca, filamentary keratitis, staphylococcal blepharokeratitis,

pneumococcal conjunctivitis, neurotrophic and vernal keratitis, recurrent erosions, and allergic and toxic keratitis.

TSPK has a very distinctive presentation, different from the presentations of each of the conditions mentioned above.

Therapy

TSPK is a self-limited disease. Therapy institution depends on patient's symptomatic tolerance. Low-dose steroids are usually first-line therapy. Some experts think steroid therapy may prolong the disease natural course.

Other therapies that have been used with good results include bandage contact lens and cyclosporine A.

Prognosis

Visual prognosis in Thygeson's superficial punctate keratitis is excellent.

Epidemiology

TSPK has no sex predilection. It usually affects patients in their second and third decades.

Cross-References

- ▶ Adenoviral Keratoconjunctivitis
- ▶ Allergic Conjunctivitis
- ▶ Dry Eye
- ▶ Keratoconjunctivitis Sicca
- ▶ Neurotrophic Keratopathy
- ▶ Recurrent Corneal Erosion
- ▶ Staphylococcus
- ▶ Vernal Conjunctivitis/Keratoconjunctivitis

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Thygeson's Superficial Punctate Keratopathy

▶ Thygeson's Superficial Punctate Keratitis

Thyroid Associated Orbitopathy (TAO)

▶ Diplopia in Graves' Ophthalmopathy

Thyroid Eye Disease

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Synonyms

Graves' eye disease; Graves' ophthalmopathy; Thyroid-associated ophthalmopathy

Definition

Thyroid eye disease (TED) is a common manifestation of a systemic autoimmune process in which autoantibodies target receptors (e.g., thyroid-stimulating hormone receptor (TSH-R)) present on thyrocytes. Systemically, these autoantibodies can induce the production of excess thyroid hormone resulting in Graves' disease and hyperthyroidism, and in the orbit, they induce secondary and inflammatory effects including glucosaminoglycan (GAG) deposition, muscle edema, and fibrosis and adipogenesis. This systemic autoimmune hyperthyroid condition is known as Graves' disease. Although TED is commonly associated with hyperthyroidism (i.e., Graves' disease), up to 20% of patients can be hypothyroid (e.g., Hashimoto's thyroiditis or treated Graves' disease), and up to 3% of TED cases are completely euthyroid.

Etiology

TED is an inflammatory and autoimmune disease, and the secondary increase in the size of the extraocular muscles and/or orbital fat results from a complex interaction between fibroblasts, inflammatory cytokines, other immune cells, autoantibodies, and other environmental (e.g., smoking) and genetic factors. The antigens that are involved in TED are still ill defined, but it is hypothesized that the thyroid and orbital tissues share a common antigen. These potential cross-reacting antigenic targets include thyroglobulin, TSH receptor, insulin-like growth factor (IGF-1) receptor, or extraocular muscle antigens.

Smoking increases both the incidence and the severity of TED, and smokers have up to five times greater risk of developing TED than nonsmokers. Genetic factors have also been thought to play a role in TED. Twenty to sixty percent of patients have a positive family history of TED, and patients may have a personal or family history of other autoimmune disorders. HLA-B8, DR3, and DQA1*0501 haplotypes may increase susceptibility to the disease, and HLA-DR β1*07 may offer protection, but the clinical significance of these genetic associations remains controversial, and we do not routinely test patients for these genetic markers.

Clinical Presentation

TED may present before the onset of thyroid dysfunction (23%), during thyroid dysfunction (39%), or when the patient is euthyroid (37%). The most frequent and distinctive lid sign in TED is eyelid retraction which affects up to 98% of patients. In addition, the temporal contour of the retracted upper lid often shows lateral flare. Lid retraction in TED may be due to sympathetic stimulation of Müller's muscle, or contraction and fibrosis of the levator muscle with secondary scarring between the lacrimal gland fascia and levator. Other findings associated with lid retraction in TED are lid lag (the eyelid lags behind eye movement on downgaze) and lagophthalmos (incomplete closure of the eyelid especially with sleep). The absence of lid retraction and lid lag should be a "red flag" clinically in patients suspected of having TED.

Many patients with TED develop dry eye-type symptoms (e.g., grittiness, foreign body sensation, lacrimation, photophobia) and are at risk for the development of secondary exposure keratopathy from the widened palpebral aperture and incomplete blinking. The orbital and periorbital inflammation and GAG deposition may cause tissue swelling in the orbit, proptosis, edema, and erythema. Enlargement and inflammatory edema of the extraocular muscles in TED can cause ocular motility dysfunction, ophthalmoplegia, and symptoms of diplopia (typically hypotropia and/or esotropia from restrictive involvement of the inferior and medial recti muscles).

The visually threatening complication of TED is compressive optic neuropathy (CON) due to extraocular muscle enlargement and compression of the optic nerve at the orbital apex. CON in TED is seen in up to 5% of clinical TED patients. In addition, some patients with TED may have an optic neuropathy from "stretching" of the optic nerve due to severe proptosis without direct CON at the orbital apex.

There are several severity scoring systems that have been proposed in TED. One of the earliest was the modified NOSPECS and more recently the clinical activity score (CAS) and the vision loss (optic neuropathy) inflammation/congestion, strabismus, and appearance/exposure (VISA) classification. These scoring systems assess lid retraction, soft tissue inflammation, proptosis, extraocular muscle involvement, corneal defects, and optic nerve compression. The NOSPECS received some criticisms leading to the development of the newer classifications. The CAS includes pain, redness, swelling, and impaired visual function. VISA classification includes subjective and objective components (vision, inflammation, strabismus, restriction, and appearance/exposure).

Diagnostics

The diagnosis of TED is typically made clinically based upon lid and orbital findings in the setting of known systemic thyroid disease. Laboratory investigation for thyroid function includes thyroid-stimulating hormone (TSH) levels, free thyroxine (T4), and free triiodothyronine (T3). Euthyroid or hypothyroid patients who have suspected TED may need further testing to confirm the autoimmune nature of the eye findings (e.g., antithyroglobulin antibodies, TSH-R antibodies (thyroid-stimulating immunoglobulin), thyroid peroxidase (TPO) antibodies, and antimicrosomal antibodies).

Orbital imaging in TED is useful for confirming the clinical diagnosis of CON by documenting the crowding by the enlarged extraocular muscles at the orbital apex. Orbital ultrasonography, CT, and MRI are all reasonable imaging options with different strengths and weaknesses. Ultrasonography, which is low cost and radiation free, can be used to measure extraocular muscle involvement and may also be useful for differentiating between myositis and TED. Orbital CT scan is the most common utilized imaging technique used in the evaluation of TED. It has the advantage of short investigation time with precise imaging of the orbital apex and the bony anatomy, is of moderate cost, and can document enlargement of extraocular muscles. It is usually indicated when CON due to TED is suspected. CT may be more sensitive than MRI in identifying extraocular muscle enlargement and is better for orbital bony anatomy if surgery is being planned. There is a theoretical risk of giving a large iodinated contrast load to patients with active hyperthyroidism, and the contrast material is not generally required for the diagnosis of TED. Orbital MRI is more sensitive than CT for soft tissue signal changes such as interstitial edema within the recti muscles in active disease but is a more expensive method for monitoring disease than CT. The main clinical caveat in ordering an imaging study in TED is to order a CT or MRI of the orbit rather than a brain study as TED does not affect the brain and a cranial imaging study could miss the orbital findings of TED.

Differential Diagnosis

1. Myositis
2. Orbital cellulitis
3. Scleritis
4. Idiopathic orbital inflammatory disease
5. Carotid cavernous fistula

Prophylaxis

Non-applicable.

Therapy

TED management should include a multidisciplinary approach. The goals of management of TED are to control symptoms efficiently and, from an endocrine perspective, to achieve a euthyroid state if possible. Patients should be counseled regarding the risks of smoking and the benefits on TED of smoking cessation.

Most patients with mild-moderate ophthalmopathy usually require no intervention other than conservative treatment, restoration of

euthyroidism, discontinuing smoking, and topical lubricants. For moderate or severe TED, corticosteroids are typically the mainstay of short-term treatment. The response rate to steroids is variable from 63% to 77% improvement in some series. IV corticosteroids have been shown to have higher efficacy and a better side effect profile in comparison to oral steroids in several studies. Many authors recommend however that the cumulative dose of IV steroids should probably not exceed 6–8 g. Corticosteroid therapy may be complicated however by multiple side effects, including decreased bone density, weight gain, liver failure, hypertension, systemic infections, gastric ulcers, and glucose intolerance. It has been our practice to recommend short-course oral or IV steroids for moderate-to-severe TED, but if no response is noted within a few weeks, we generally taper the steroids quickly to avoid systemic side effects. We also use corticosteroids in patients with CON from TED prior to orbital decompression.

Radiation therapy has also been used in the management of TED. Radiotherapy is thought to have both a nonspecific anti-inflammatory effect and a predilection for lymphocyte effects. The most common dose is 20 Gy per orbit distributed in divided daily fractions over a 2-week period. Orbital radiotherapy may be associated with transient exacerbation of inflammation, which may be reduced with concomitant steroid use. The efficacy of radiotherapy remains controversial however, and there is conflicting data from the literature in sham radiation therapy-controlled trials. Several studies have shown that radiotherapy in combination with steroids may produce a better clinical response rate than either therapy alone.

Other steroid sparing immunosuppressive drugs have been used anecdotally for TED. Cyclosporine has been evaluated in the management of TED but was not as effective as oral steroids in reducing inflammation in one series. However, the combination of oral steroid and cyclosporine may be superior to oral steroids alone. Rituximab is an anti-CD20 chimeric, humanized, monoclonal antibody that targets mature B cells. It has been shown in anecdotal reports to decrease CAS in moderate-to-severe TED resistant to IV steroids. Other treatment modalities that have been shown in scattered reports to decrease CAS include antitumor necrosis-α antibody (TNFα), intravenous immunoglobulin (IVIG), plasma filtration, colchicine, and rapamycin. Unfortunately, there are no randomized control trials evaluating the efficacy of these treatment modalities.

The indications for surgical intervention in TED include optic neuropathy (typically CON but also proptosis-related stretch optic neuropathy in TED), severe ophthalmoplegia/diplopia, marked proptosis/corneal exposure, and reconstructive/cosmetic issues. Surgical procedures include orbital decompression for CON, strabismus repair, and correction of eyelid abnormality. Traditionally, if a patient with TED requires all three surgeries, then orbital decompression is performed initially, followed by strabismus surgery, and then eyelid repair as orbital surgery can cause or worsen strabismus, and strabismus surgery can affect the lid position. Some patients require surgery in the order of most importance and symptom relief. Most decompression surgery is performed when the patient has been in stable inactive state for at least 6 months. However, urgent decompression may be needed for CON or severe proptosis refractory to other treatment. Orbital fat decompression has also been used to reduce proptosis in TED.

Prognosis

Fortunately, moderate-to-severe (6%) and sight threatening TED (0.8%) complications are uncommon at presentation, and only 3–5% of TED patients develop CON. In addition, most patients (>80%) with no TED at baseline do not develop TED on follow-up, but this is variable and unpredictable.

Epidemiology

TED is the most common disease affecting the orbit. It is present in up to 40% of patients with

Graves' disease. It usually presents in the third to fifth decade and is more common in women. The estimated incidence is 16 per 100,000 person years in females and 3 per 100,000 person years in males.

Although TED disease is more common in women, the proportion of men increases as severity of disease increases from 9.3:1 in mild TED to 1.4:1 in severe TED. The risk and severity of TED may be increased by tobacco use, genetics, type of hyperthyroidism treatment, TSH-R Ab levels, advanced age, and stress. Smoking is the strongest modifiable risk factor for TED. Myasthenia gravis has been found to be up to 50 times more common in TED; it also may signify a worse prognosis. The diagnosis of concomitant MG should be suspected in TED when there is concomitant ptosis (rather than lid retraction) or exotropia (rather than esotropia or hypotropia).

Cross-References

- ▶ Graves' Disease
- ▶ Graves Ophthalmopathy
- ▶ Ring Sign, in Idiopathic Orbital Inflammation
- ▶ Orbital Cellulitis
- ▶ Scleritis

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Thyroid Eye Disease (TED)

- ▶ Diplopia in Graves' Ophthalmopathy

Thyroid-Associated Ophthalmopathy

- ▶ Thyroid Eye Disease

Thyroid-Associated Orbitopathy

- ▶ Graves' Disease

Tight Orbit

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Synonyms

Orbital compartment syndrome

Definition

Orbital compartment syndrome is a rare, but emergent, acute rise in orbital pressure that may to damage of ocular and intraorbital structures causing irreversible blindness.

Etiology

Tight orbit is most commonly secondary to an orbital trauma, surgery, or local injection causing a retrobulbar hematoma. It may also be seen with fulminant orbital cellulitis, intraorbital abscess, orbital emphysema, inflammation, or tumor. Less commonly it can be seen following large-volume resuscitation after burn injury, spontaneous bleeding from vascular anomalies, extravasated contrast material, and position-dependent edema causing an acute rise in orbital pressure.

Clinical Presentation

Signs and symptoms include decreased visual acuity, afferent pupillary defect, periorbital pain, ocular pain, diplopia, restricted ocular motility, proptosis, ecchymosis, chemosis, decreased visual fields, optic disc edema, retinal venous congestion, central retinal artery pulsation, pale optic disc, and a cherry-red macula.

Diagnosis

Diagnosis is primarily clinical examining visual acuity, pupillary response, intraocular pressure, extraocular motility, and fundoscopic examination. In the setting of rapidly progressing signs and symptoms with vision loss and an afferent pupillary defect, there should be no delay for imaging or testing. When clinically appropriate, imaging with a CT or MRI of the orbits may confirm the diagnosis.

Differential Diagnosis

Idiopathic orbital inflammation
Thyroid eye disease
Ruptured dermoid cyst
Orbital neoplasm
Direct injury from surgical dissection
Anterior ischemic optic neuropathy
Endophthalmitis
Globe rupture

Prophylaxis

Avoiding nose blowing, Valsalva, or coughing may minimize the risk of orbital hemorrhage or emphysema in patients with orbital trauma.

Avoiding platelet inhibitors and blood thinners when possible in patients undergoing orbital surgery. Intraoperative meticulous hemostasis should be achieved and excision of orbital fat should be performed under direct visualization in order to avoid excess traction into deep orbital fat.

Gentle awakening for general anesthesia with adequate pain and nausea control and suppression of the cough reflex to minimize straining.

Prompt antibiotics or anti-inflammatory agents in cases of orbital cellulitis or inflammation may minimize orbital pressure.

Therapy

Treatment of acute vision loss with orbital compartment syndrome should be done emergently with lateral canthotomy and inferior cantholysis for orbital decompression. If it fails to relieve orbital tension and restore perfusion to the optic nerve and retina, superior cantholysis should be performed. If there is no improvement within a few minutes, then the orbital septum should be divided from its attachment to the orbital rims. Other indications for decompression include intraocular pressure (IOP) greater than 40 mmHg, relative afferent pupillary defect, ophthalmoplegia, cherry-red macula, and optic nerve head pallor.

In postoperative tight orbit due to orbital hemorrhage decompressing the surgical incision, evacuating the hematoma and cauterizing bleeding vessels.

In most patients, the lateral canthus will heal spontaneously; however, if a cosmetic deformity or lower lid ectropion persists, repair can be performed.

Pharmacologic therapy with ocular hypotensive medications including beta-blockers (i.e., timolol), alpha-agonists (i.e., brimonidine), and carbonic anhydrase inhibitors (i.e., dorzolamide or acetazolamide). May also consider corticosteroids to decrease inflammation and antimicrobials for infectious etiology.

Prognosis

Delaying treatment with orbital decompression is more likely to result in permanent vision loss.

Epidemiology

Tight orbit is rare, but occurs most commonly following orbital trauma or postoperative complications of eye surgery.

Cross-References

- ▶ Cantholysis
- ▶ Lateral Canthotomy
- ▶ Orbital Compartment Syndrome
- ▶ Retrobulbar Hemorrhage

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Tissue Adhesives, Cyanoacrylate, for Anterior Segment

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Synonyms

Adhesive; Glue

Indications

Corneal perforations <3 mm diameter, fixation of conjunctival graft during pterygium surgery, fixation of amniotic membrane graft.

Contraindications

Active infection; large perforations; allergy to glue constituents.

Techniques and Principles

The use of tissue adhesives in ophthalmology can be dated back to 1950 (Tassman 1950; Bhatia 2006). A variety of synthetic and biological tissue adhesives are available; however, only a few of these are being used on an off-label basis. Ocular adhesives can be grouped as (1) cyanoacrylate based, (2) fibrin/blood based, and (3) polyethylene glycols.

Cyanoacrylate-Based Adhesives

Cyanoacrylate is the most commonly used ocular tissue adhesive possibly related to its ease of availability and low cost as compared to other adhesives. Although the initial use was limited to closure of corneal perforation, they have been used for cataract wound closure, leaking blebs, retinal detachment surgery, scleral reinforcement, attachment of muscles to ocular prosthetics, temporary tarsorrhaphy, punctal occlusion, blepharoplasty, and skin closure after DCR.

Available preparations of corneal glue for clinical use include the following:

- Indermil (butyl-2-cyanoacrylate; Sherwood, Davis and Geck, St Louis, MO, USA)
- Histoacryl (butyl-2-cyanoacrylate; B. Braun, Melsungen, Germany)
- Histoacryl Blue (*N*-butyl-2-cyanoacrylate; B. Braun)
- Nexacryl (*N*-butyl-cyanoacrylate; Closure Medical, Raleigh, NC, USA)
- Dermabond (2-octyl-cyanoacrylate; Closure Medical)

Commercially available "super glue" (methyl-2-cyanoacrylate) appears to be more toxic than the other acrylate derivatives.

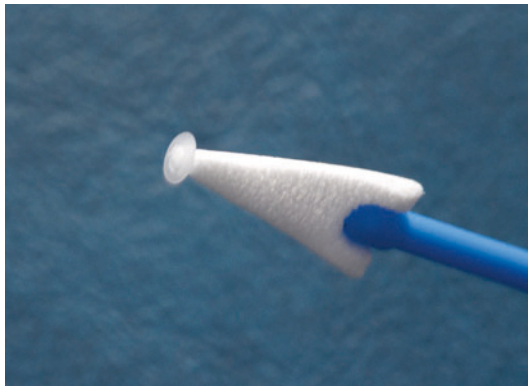
Cyanoacrylate glue provides a bacteriostatic effect at the time of application. It can inhibit polymorphonuclear neutrophil migration, therefore preventing or delaying stromal melting. Cyanoacrylate glue can be used for corneal perforations

related to herpes simplex, keratoconjunctivitis sicca, alkali burns, radiation keratitis, rheumatoid arthritis, and Stevens-Johnson syndrome. In cases with corneal perforation <3 mm in diameter, direct early application of cyanoacrylate adhesive to the ulcer bed and adjacent basement membrane plus a bandage contact lens is effective in the interruption of progressive corneal stromal melting. A small amount of glue should be applied in a controlled manner, avoiding excessive spillage. An alternative method involves creation of a mesh with 10-0 nylon sutures at the site of corneal perforation before the application of glue.

Surgical Technique

Glue application should be performed in a sterile environment preferably under an operating microscope. Application can be performed in selected cases on slit lamp as well. A 2- to 3-mm dermatological punch is used to trephine a circular disk from a sterile disposable drape (Fig. 1). A small amount of chloramphenicol ointment or K-Y jelly is placed on the flat end of a cotton-tipped applicator, and the disk is then stuck onto the ointment (Fig. 2). A few drops of topical anesthesia are applied to the eye. A non-compressing lid speculum is used to separate the lids gently. The loose epithelium and necrotic tissue around the perforation site are removed carefully. The perforation site should be as dry as possible for the glue to stick. If the anterior chamber is flat, a small amount of air or viscoelastic may be injected to form the chamber to avoid incarceration of iris or other tissues to the adhesive. One drop of adhesive is then applied to the trephined disk, and with further drying, the adhesive is directly applied to the area of perforation. The polymerization process will take place in several minutes. If a small leak remains, additional applications adjacent to the existing plug may be applied. Multiple reapplications are not recommended because this will enlarge the defect. After solidification, the area should be dried and examined with fluorescein dye for further leaks. A bandage contact lens is applied at the end of the procedure. The patient should be examined a few minutes later to ensure the glue/disk contact lens complex is in situ and the anterior chamber is deepening. A protective shield should be placed.

Tissue Adhesives, Cyanoacrylate, for Anterior Segment, Fig. 1 Corneal gluing set



Tissue Adhesives, Cyanoacrylate, for Anterior Segment, Fig. 2 Plastic, circular disk stuck to the tip of a sponge with chloramphenicol ointment

The postoperative treatment includes topical antibiotic therapy and an aqueous suppressant. In cases of infectious perforations, patients should continue their medications. Ideally the glue should remain in position for as long as possible, but careful monitoring is required because the risk of glue dislodgement and re-perforation is high.

Fibrin-Based Adhesives

The Food and Drug Administration has approved the use of fibrin glue for hemostasis; however, the ophthalmic use of fibrin glue has increased tremendously in the past few years. It has been used for closure of impending as well as frank corneal perforations and penetrating corneal transplant wounds, sealing of traumatic lens capsule lacerations, conjunctival closure after surgery, lamellar keratoplasty, repair of leaking blebs, and wound closure in blepharoplasty. It is being widely used to anchor amniotic membrane grafts as well as conjunctival autografts after pterygium surgery.

The main advantages of fibrin tissue adhesives over cyanoacrylate-based tissue adhesives in that they solidify quickly and cause less discomfort. As compared to cyanoacrylate glue, biological glues start to degrade faster and have no bacteriostatic effects. There is a risk of transmission of prion/viral diseases with the use of bovine products in its constituents. The fibrinogen in commercial preparations is vapor-heated and freeze-dried to minimize the risk of pathogen transmission.

Outcomes

The outcomes of corneal gluing have been reported to be very promising especially if used early in the course of diseases. Successful corneal gluing may obviate the need for other surgical treatments. Jhanji et al. (2011) have shown improved visual outcomes with reduced enucleation rate. However, another report showed that the success of cyanoacrylate corneal gluing might not be high in cases with herpetic corneal perforations (Moorthy et al. 2010).

Fibrin glue has been increasingly used in pterygium surgery to fix the conjunctival graft on bare sclera. The grafts secured with fibrin glue during pterygium surgery were found to be stable. The use of fibrin glue was associated with less inflammation as compared to sutures (Srinivasan et al. 2009).

Complications

Complications have been reported with the use of fibrin-based adhesives after pterygium surgery, most commonly graft dehiscence or loss. A potential complication for fibrin glue is viral transmission although it has not been reported so far.

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TLSS

► Transient Light-Sensitivity Syndrome

Tobacco-Alcohol Amblyopia

► Toxic Optic Neuropathy
► Toxic/Nutritional and Hereditary Optic Neuropathy

Tonic Pupil (Adie's Pupil), Pharmacological Testing for

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Synonyms

Adie syndrome; Adie's tonic pupil; Holmes-Adie syndrome; Little old Adie's pupil

Definition

The tonic pupil is characterized by a pupil that poorly reacts to light but reacts better and tonically to near. The tonic pupil can be caused by damage to the parasympathetic innervation of the ciliary ganglion and postganglionic fibers to the eye.

Etiology

Damage to the parasympathetic ciliary ganglion or the postganglionic nerves produces a tonic pupil. After damage in this location, denervation supersensitivity develops. Because 30 times more axons innervate the ciliary body than the pupil, reinnervation may cause axons to accidently reroute to the pupil rather than to the ciliary body. This aberrant reinnervation produces accommodation-induced tonic near reaction. Adie's pupil is typically regarded as idiopathic. Up to 20% of Adie's pupils present bilaterally with an annual rate of 4% bilateral involvement/year (Figs. 1 and 2).

Clinical Presentation

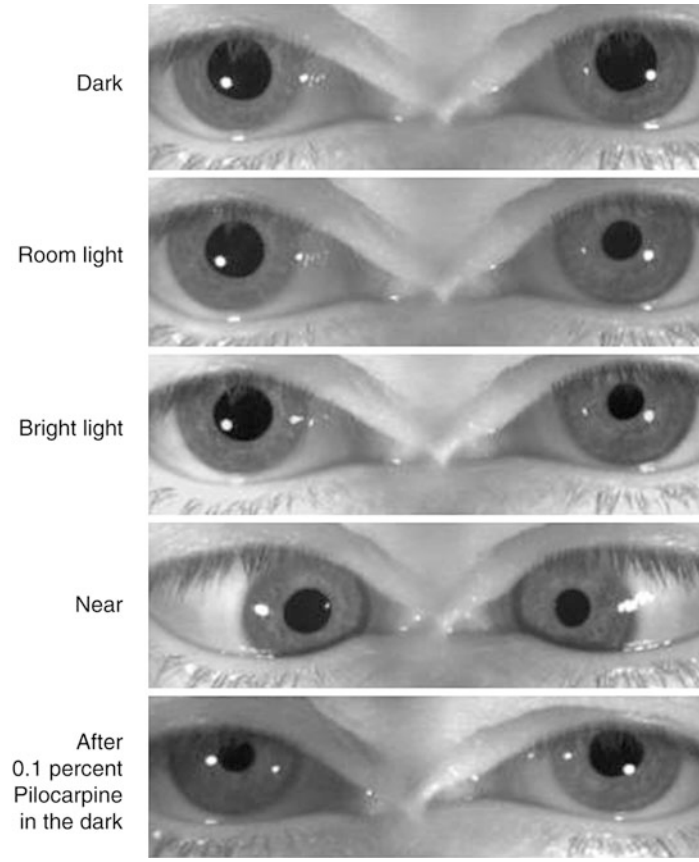
Patients with the tonic pupil usually present with anisocoria. On examination, the tonic pupil shows poor or no pupillary light reaction but a better near reaction (i.e., light-near dissociation).

Diagnostics

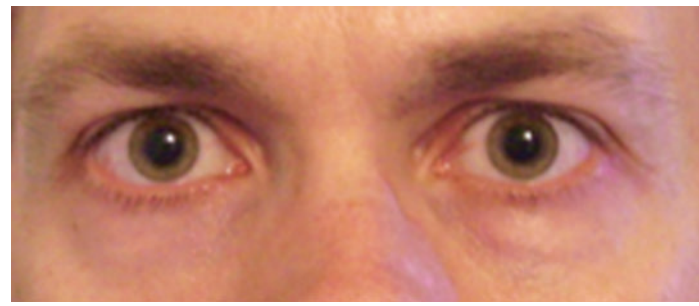
The anisocoria in the tonic pupil is worse in the light and better in the dark. Examining old photographs can help in distinguishing whether the anisocoria is an acute or chronic process.

Pharmacological Testing

Topical 0.1% pilocarpine often reveals cholinergic supersensitivity in the tonic pupil. Pilocarpine should be applied in both eyes with the fellow eye



Tonic Pupil (Adie's Pupil), Pharmacological Testing for, Fig. 1 Adie's pupil in R. eye – (**a**, **b**) anisocoria greater in the light than in the dark; (**c**) improved constriction to light-near dissociation than to light; (**d**) improved constriction after 0.1 % pilocarpine application due to denervation supersensitivity (from the University of Iowa Neuro-ophthalmology division)



Tonic Pupil (Adie's Pupil), Pharmacological Testing for, Fig. 2 Bilateral Adie's pupil (National Institute of Neurological Disorders and Stroke 2013)

acting as a control. Pupillary constriction to low-dose pilocarpine is evidence for denervation supersensitivity. Only 80% of patients with Adie's pupil however demonstrate cholinergic supersensitivity. In addition, cholinergic supersensitivity has also been noted in patients with CN III preganglionic lesions.

Differential Diagnosis

Local orbital syndrome and autonomic neuropathies (e.g., Charcot-Marie Tooth disease and Guillain-Barre syndrome), orbital infection and inflammation, trauma, surgery local anesthesia due to an inferior dental block, or retrobulbar

alcohol injection can present with a tonic pupil. Damage to the ciliary ganglion including surgery and laser therapy may result in a tonic pupil as well.

Prophylaxis

There is no prophylaxis for Adie's pupil.

Therapy

Most patients do not require treatment; however some patients with tonic pupil may benefit from reassurance, bifocal glasses (unilateral frosted or unequal power), or intermittent as needed low-dose pilocarpine.

Prognosis

Most tonic pupils are Adie's pupils and thus are benign and only require supportive care. **In many cases**, **the pupil may constrict even further over time**, **leading to a "little old Adie's" pupil**.

Epidemiology

Idiopathic Adie's pupils predominate in females with a 2.6:1 ratio. The mean age is 32 years, although it has been found to appear in all ages. Adie's pupils occur in about 0.2% of the population at any given time.

Cross-References

► Adie's Pupil
► Anisocoria

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Topical Anesthesia

► Topical Anesthesia in Eye Surgery

Topical Anesthesia in Eye Surgery

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Synonyms

Surface anesthesia; Topical anesthesia

Definition

Application of local anesthetics to the surface in order to block nociception. In ophthalmology, this is used for anesthesia of the cornea and the anterior part of the globe.

Indication

There is a wide indication for topical anesthesia (TA). It ranges from foreign body extraction to cataract surgery, keratoplasty, and glaucoma surgery.

Contraindication

Several groups of contraindications have to be distinguished:

Medical contraindications: These include allergy to anesthetics as well as abuse of local anesthetics to treat chronic ocular pain. This may result in corneal ulceration.

Surgical contraindications: Topical anesthesia does only block nociception within the anterior part of the globe, i.e., corneal, conjunctival, and anterior scleral anesthesia. Procedures that involve rather posterior structures are therefore not subject to topical anesthesia. Additionally, the durance of local anesthesia is somewhat shorter than in needle block anesthesia. In case of prolonged surgery time (due to procedure or inexperienced surgeon) needle block anesthesia is therefore of advantage.

Topical anesthesia does not cause motor block. Therefore, full mobility of globe as well as patient movements due to increased discomfort are limitations of TA. TA should therefore be restricted to planned and easy procedures in otherwise healthy patients. Procedures should be performed by experienced surgeons.

Use and Dosage

Local anesthetic is put on the surface of the eye either as drop or gel until a sufficient anesthesia is achieved. Some authors also perform intracameral anesthesia in order to aid topical anesthesia.

Adverse Reactions

Local anesthetics – even though only in contact with conjunctiva may cause allergic reactions. Long-term use to treat ocular pain is strictly contraindicated. In rare cases, corneal epithelial, endothelial, and retinal toxicity have been described.

Interactions

Local anesthetics may interact with other topical drugs, for example, antiglaucomatosa, if applied shortly thereafter.

Cross-References

- ▶ Anesthesia (Anesthetics), Local
- ▶ Cataract Surgery
- ▶ Retrobulbar Block
- ▶ Subtenon's Anesthesia
- ▶ Topical Anesthesia

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Topography (Corneal)

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See ▶ Corneal Topography.

Total Color Blindness

▶ Achromatopsia (Rod Monochromatism), Gene Defects Causing

Toxic Anterior Segment Syndrome

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Synonyms

TASS

Definition

Sterile inflammatory reaction of unknown incidence that can occur after anterior segment surgery.

Etiology

Administration of solutions of inappropriate chemical composition during anterior segment surgery.

Various entities have been shown to cause toxic anterior segment syndrome. These include, but are not limited to, endotoxin; denatured ophthalmic viscosurgical devices; preservatives such as benzalkonium chloride, bisulfites, and metabisulfites; heavy metal residue; fine-matter particulates; and substances introduced into the anterior chamber that are at a pH or concentration that is toxic to the endothelial cells. In addition, residue of materials used in the cleaning and sterilization of ophthalmic instruments are a cause of toxic anterior segment syndrome.

Occurrence

After administration of solutions of inappropriate chemical composition during surgery, a sterile anterior chamber inflammation develops 12–48 h after surgery. Endophthalmitis as a differential diagnoses should be ruled out by bacterial cultures. Toxic anterior segment syndrome responds to steroid treatment. Patients may present with blurred vision and pain, but most cases are asymptomatic. Clinically, edema of the cornea can be observed. Inflammatory cells with hypopyon, fibrous reaction, and aqueous flare may be found as a consequence of the breakdown of the blood-aqueous barrier. Inflammation of the trabecular meshwork may cause a rise of intraocular pressure. Prognosis is variable according to the degree of toxic damage.

Classification

Cases limited to the corneal endothelium are called toxic endothelial cell destruction syndrome.

Cross-References

▶ Cataract Surgery
▶ Endophthalmitis

Further Reading

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Toxic Optic Neuropathy

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Synonyms

Chemical-induced optic neuropathy; Drug-induced optic neuropathy; Nutritional amblyopia; Tobacco-alcohol amblyopia

Definition

Visual impairment due to optic nerve damage from toxic optic neuropathy (TON). TON typically preferentially affects the papillomacular bundle bilaterally by a nutritional deficiency or accumulation of a toxic substance to the optic nerve.

Etiology

Causes of nutritional/toxic include:

I. Nutritional deficiency including commonly deficiencies in vitamin B_{12} (cyanocobalamin) and folate as well as less commonly other vitamins (e.g., thiamine, pyridoxine, niacin, riboflavin)
II. Substance/drug toxicity
    1. Drug-induced (e.g., most commonly ethambutol but also isoniazid, linezolid, disulfiram, tamoxifen, quinine, chloramphenicol, amiodarone, dapsone, 5-fluorouracil).
    2. Chemical-(toxin) induced (e.g., methanol, ethylene glycol)
    3. Heavy metal poisoning (e.g., chronic lead exposure, thallium, arsenic)

Poor diet (e.g., alcohol consumption, strict vegan diet, eating disorder), bariatric or other gastrointestinal surgery (partial or complete ileum resection) and autoimmune (e.g., pernicious anemia) disorders can cause vitamin deficiency states. Pernicious anemia is an autoimmune disease that produces autoantibodies against intrinsic factor that leads to impaired vitamin B_{12} absorption. Like vitamin B_{12} deficiency, a poor diet and alcohol abuse can also lead to separate or concomitant folate deficiency.

Ethambutol (EMB) is antituberculosis (TB) agent and is also used against other mycobacterium (e.g., mycobacterium avium complex). EMB causes a dose-dependent toxic optic

neuropathy bilaterally. The incidence of EMB-induced optic neuropathy ranges from 1% to 5% and the risk factors associated with toxicity include diabetes mellitus, chronic renal failure, alcoholism, elderly patients, children, other concomitant ocular defects, the presence of EMB-induced peripheral neuropathy, and a dose greater than 15 mg/kg/day. Other toxic optic neuropathies are usually diagnosed by an appropriate exposure history.

Clinical Presentation

Nutritional/toxic optic neuropathy typically presents as a, painless, slowly progressive bilateral, simultaneous generally symmetric loss of central vision often preceded or accompanied by color vision deficits (dyschromatopsia). Since the papillomacular bundle is predominantly affected by these disorders, patients typically present with central or cecocentral scotoma, dyschromatopsia, and normal disk appearance at onset but eventual temporal pallor of the optic disks OU. The color vision deficits can present early due to the high concentration of color sensitive cones within the macula. Due to the systemic nature of the problem, the vision loss is typically bilateral, central, and symmetric. Therefore, typically no relative afferent visual field defect (RAPD) is present, but the pupillary response may be sluggish bilaterally. An RAPD may be present, however, in bilateral but asymmetric disease.

Many of the drug-induced toxic neuropathies present with similar clinical symptoms. EMB produces a dose-dependent toxic optic neuropathy in which patients often present with visual symptoms at 2–8 months after initiation of the drug. Some believe that the earliest sign of visual dysfunction is dyschromatopsia (especially blue yellow). As in other toxic-nutritional optic neuropathies, the most common visual field defects are bilateral central or cecocentral scotomas. However, other visual field defects are possible as well such as peripheral defects (e.g., peripheral periaxial toxicity) or even pseudobitemporal hemianopsia from break out of the central or cecocentral scotoma into the temporal periphery bilaterally. Patients with pseudobitemporal hemianopsia from EMB toxicity, however, present with concomitant loss of central visual field and visual acuity OU.

Other causes of toxic optic neuropathy include methanol or less commonly ethylene glycol poisoning. Unlike in most other nutritional and toxic optic neuropathies, chemical-induced optic neuropathies (i.e., methanol or ethylene glycol poisoning) present with an acute, bilateral and severe vision loss sometimes progressing to complete blindness. The history of exposure is usually diagnostic in these cases.

Diagnostics

The first step in diagnosing a patient with suspected toxic-nutritional optic neuropathy is a detailed history of the patient's medical/surgical history (e.g., gastric bypass, abdominal surgery), diet (e.g., alcohol intake, eating disorder, vegan diet), and medications (e.g., EMB, other). A comprehensive review of systems should also be performed including symptoms and signs of toxicity (e.g., peripheral sensory symptoms, anemia, mental status changes, nyctalopia, and gait disturbance).

The examination should include a complete eye exam, but formal visual field testing is crucial to show the specific type of visual field defect (e.g., central or cecocentral scotoma with preservation of peripheral fields or less commonly peripheral visual field loss in periaxial forms). Fundus examination is typically normal in toxic-nutritional and hereditary optic neuropathy at onset but may eventually show temporal pallor OU. Optical coherence tomography (OCT) might demonstrate retinal nerve fiber layer dropout in the papillomacular bundle OU over time.

Suggested lab testing depending on the clinical history and exam might include: complete blood

count (CBC) with differential, serum B_{12}, serum and red blood cell (RBC) folate and if indicated other vitamin levels. If the level of vitamin B_{12} is low or borderline, obtaining plasma homocysteine and methylmalonic acid levels can confirm more long-standing B_{12} deficiency states. Even with borderline B_{12} levels, both homocysteine and methylmalonic acid can be elevated – proving a functional deficiency of the nutrient. If only homocysteine is elevated, then a concomitant folate deficiency may also be present. These findings are due the fact that cobalamin (B_{12}) is a cofactor in the conversion of homocysteine to methionine as well as methylmalonyl-CoA to succinyl-CoA. Folate is involved in the methylation of cobalamin to methylcobalamin that in turn methylates homocysteine to methionine. Folate is not involved in the conversion of methylmalonyl-CoA to succinyl-CoA.

Patients starting on ethambutol or isoniazid should receive a baseline initial screening ophthalmic evaluation including formal visual field testing, color vision, dilated fundoscopic exam, visual acuity, and other baseline screening modalities (e.g., optical coherence tomography (OCT) of the optic nerve). OCT analysis of the retinal nerve fiber layer of the optic disk in EMB toxic optic neuropathy may show nerve fiber layer thinning that can appear prior to obvious changes in appearance of the fundus. Although generally an acute toxicity, retinal examination of patients with methanol poisoning can show edema of the peripapillary nerve fiber layer and optic disk that eventually leads to bilateral and severe optic atrophy.

Patients with clinical symptoms consistent with a proven diagnosis of toxic/nutritional or hereditary optic neuropathy may still require further testing including a neuroimaging study and preferably magnetic resonance imaging (MRI) of brain and orbit with and without contrast with fat saturation. Some patients with progressive unexplained optic neuropathy may need lumbar puncture and further evaluation for infectious, inflammatory, ischemic, infiltrative, or paraneoplastic etiologies. Leber hereditary optic neuropathy (LHON) mitochondrial DNA mutation testing and heavy metal screening could be considered even in patients with B_{12} or folate deficiency as some patients have multifactorial disease.

Differential Diagnosis

1. Compressive optic neuropathy/infiltrative optic neuropathy
2. Maculopathy/macular dystrophy
3. Bilateral inflammatory/infectious e.g., syphilis
4. Bilateral demyelinating optic neuropathy
5. Radiation optic neuropathy

Prophylaxis

Non applicable

Therapy

The first step in the treatment of nutritional deficiency is vitamin replacement. In addition, the ophthalmologist should recommend discontinuation of smoking/alcohol use. When drug or substance toxicity is suspected, the offending agent (e.g., EMB) should be discontinued but only in consultation with the prescribing physician. Treatment should then depend on the cause of the disorder. Treatment for chemical-induced optic neuropathies includes correction of the concomitant acute systemic deficiencies and correction of electrolyte abnormalities including metabolic acidosis with administration of IV sodium bicarbonate. In methanol poisoning, although ethanol can also be administered to compete with the metabolism of methanol into its more destructive and toxic by-products, fomepizole is generally considered first line. Hemodialysis is indicated if methanol is detected at blood levels over 50 mg/dL.

Treatment for isoniazid-induced optic neuropathy includes administration of pyridoxine 25–100 mg/day to help stabilize or possibly reverse the neuropathy and may occur independent simultaneously with EMB toxicity.

Prognosis

Depending on the duration and severity of the findings, many cases of nutritional optic neuropathy have a favorable prognosis. However, permanent optic atrophy or temporal disk pallor can occur depending on the timing of diagnosis and start of treatment. Patients usually see improvement within 1–2 months of nutritional supplementation although in some individuals' improvement may not occur for 1 year.

Patients with ethambutol toxicity may still recover normal visual function after drug discontinuation. However, if significant optic disk pallor is already present, visual recovery is less likely to occur. Thus, early recognition and discontinuation of the drug are critical before the development of irreversible optic atrophy.

Cross-References

- ▶ Demyelinating Optic Neuropathy
- ▶ Inflammatory Eye Disease
- ▶ Macular Dystrophy
- ▶ Methanol, Optic Neuropathy
- ▶ Optic Neuropathy

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Toxic Ulcerative Keratopathy

▶ Ulcerative Keratopathy, Toxic

Toxic/Nutritional and Hereditary Optic Neuropathy

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Synonyms

Autosomal dominant optic atrophy; Autosomal recessive optic atrophy; Chemical-induced optic neuropathy; Drug-induced optic neuropathy; Leber's hereditary optic neuropathy (LHON); Nutritional amblyopia; Tobacco-alcohol amblyopia

Definition

Visual impairment due to optic nerve damage that preferentially affects the papillomacular bundle bilaterally by a nutritional deficiency, accumulation of a toxic substance to the optic nerve, or an inherited genetic mutation that may act independently or together.

Etiology

Causes of nutritional/toxic and hereditary optic neuropathies include:

I. Nutritional deficiency including deficiencies in vitamin B12 (i.e., cyanocobalamin), folate, and other vitamins (e.g., thiamine, pyridoxine, niacin, riboflavin)
II. Substance/drug toxicity
    1. Drug induced (e.g., most commonly ethambutol but also isoniazid, linezolid, disulfiram, tamoxifen, quinine, chloramphenicol, amiodarone, dapsone, 5-fluorouracil, etc.)
    2. Chemical (toxin)-induced (e.g., methanol, ethylene glycol)
    3. Heavy metal poisoning (e.g., chronic lead exposure, thallium, arsenic)
III. Hereditary
    1. Leber's hereditary optic neuropathy (LHON)
    2. Autosomal dominant optic atrophy (ADOA), commonly Kjer optic neuropathy
    3. Autosomal recessive (infantile) optic atrophy (AROA)
    4. Rare other inherited forms (X-linked)

While nutritional optic neuropathies are often associated with multiple vitamin deficiencies, vitamin B12 and folate are the most common causes. Poor diet (e.g., alcohol consumption, strict vegan diet, eating disorder), bariatric or other gastrointestinal surgery (partial or complete ileum resection) and autoimmune (e.g., pernicious anemia) can cause vitamin deficiency states. Pernicious anemia is an autoimmune disease that produces autoantibodies against intrinsic factor that leads to impaired vitamin B12 absorption. Like vitamin B12 deficiency, a poor diet and alcohol abuse can also lead to separate or concomitant folate deficiency.

Ethambutol (EMB) is an antituberculosis (TB) agent and is also used against other mycobacteria (e.g., mycobacterium avium complex). EMB cause a dose-dependent toxic optic neuropathy bilaterally. The incidence of EMB-induced optic neuropathy ranges from 1% to 5%, and the risk factors associated with toxicity include diabetes mellitus, chronic renal failure, alcoholism, elderly patients, children, other concomitant ocular defects, the presence of EMB-induced peripheral neuropathy, and a dose greater than 15 mg/kg/day. Other toxic optic neuropathies are usually diagnosed by an appropriate exposure history.

LHON is a rare disease caused by the inheritance of maternal mitochondrial DNA mutations (95% of LHON) at positions 11778, 14484, or 3460, predominately affecting young adult males. Production of dysfunctional adenosine triphosphate (ATP) occurs as a result of these mutations, leading to defective oxidative phosphorylation in the highly energy-dependent optic nerve. LHON can be precipitated by many environmental factors including nutritional deprivation, alcohol consumption, smoking, acute illness, and psychological stress. ADOA is the most common cause of the hereditary optic neuropathies with an estimated disease prevalence of 1:12,000–1:50,000. Other less common hereditary optic neuropathies are AD, AR, and X-linked.

Clinical Presentation

Nutritional/toxic optic neuropathy typically presents as a painless, slowly progressive bilateral, simultaneous generally symmetric loss of central vision often preceded or accompanied by color vision deficits (dyschromatopsia). Since the papillomacular bundle is predominantly affected by these disorders, patients typically present with central or cecocentral scotoma, dyschromatopsia, and normal disk appearance at onset but eventual temporal pallor of the optic disks OU. The color vision deficits can present early due to the high concentration of color-sensitive cones within the macula. Due to the systemic nature of the problem, the vision loss is typically bilateral, central, and symmetric. Therefore, typically no relative afferent visual field defect (RAPD) is present, but the pupillary response may be sluggish bilaterally. An RAPD may be present however in bilateral but asymmetric disease.

Many of the drug-induced toxic neuropathies present with similar clinical symptoms. EMB produces a dose-dependent toxic optic neuropathy in which patients often present with visual symptoms at 2–8 months after initiation of the drug. Some believe that the earliest sign of visual dysfunction is dyschromatopsia (especially blue-yellow). As in other toxic-nutritional optic neuropathies, the most common visual field defects are bilateral central or cecocentral scotomas. However, other visual field defects are possible as well such as peripheral defects (e.g., peripheral or periaxial toxicity) or even pseudo-bitemporal hemianopia from breakout of the central or cecocentral scotoma into the temporal periphery bilaterally. Patients with pseudo-bitemporal hemianopia from EMB toxicity however present with concomitant loss of central visual field and visual acuity OU.

Other causes of toxic optic neuropathy include methanol or less commonly ethylene glycol poisoning. Unlike in most other nutritional and toxic optic neuropathies, chemical-induced optic neuropathies (e.g., methanol or ethylene glycol poisoning) present with an acute, bilateral, and severe vision loss sometimes progressing to complete blindness. The history of exposure is usually diagnostic in these cases.

Patients with LHON are typically young males (aged 11–30) who present with sudden, painless, bilateral simultaneous, or rapidly sequential central/cecocentral scotomas. In contrast, the other hereditary optic neuropathies (e.g., ADOA) classically begin during childhood, often insidiously, and then the visual loss OU progressively worsens throughout life. It characteristically presents with central or centrocecal scotomas OU with decreased color vision and is often detected by childhood vision screening exams as mild reduction in visual acuity. Hereditary optic neuropathies can be associated with other neurologic deficits such as congenital or progressive deafness or ataxia. Patients with autosomal recessive (infantile) optic atrophy (AROA) typically present with much more severe visual loss OU with nystagmus at birth or within 2 years of age. AROA can also be associated with congenital deafness, spastic quadriplegia, and dementia.

Diagnostics

The first step in diagnosing a patient with suspected toxic-nutritional optic neuropathy is a detailed history of the patient's medical/surgical history (e.g., gastric bypass, abdominal surgery), diet (e.g., alcohol intake, eating disorder, vegan diet), and medications (EMB, other). A family history is crucial for detecting hereditary optic neuropathies and for describing the pedigree to define the inheritance pattern. Many patients with LHON however have no family history of visual loss. A comprehensive review of systems should also be performed including symptoms and signs of toxicity (e.g., peripheral sensory symptoms, anemia, mental status changes, nyctalopia, and gait disturbance).

The examination should include a complete eye exam, but formal visual field testing is crucial to show the specific type of visual field defect (central or cecocentral scotoma with preservation of peripheral fields). Fundus examination is typically normal in toxic-nutritional and hereditary optic neuropathy at onset but may eventually show temporal pallor OU. Optical coherence tomography (OCT) might demonstrate retinal nerve fiber layer drop out in the papillomacular bundle OU over time.

Suggested lab testing depending on the clinical history and exam might include complete blood count (CBC) with differential, serum B_{12}, serum and red blood cell (RBC) folate, and syphilis serology. If the level of vitamin B12 is low or borderline, obtaining plasma homocysteine and methylmalonic acid levels can confirm more long-standing B12 deficiency states. Even with borderline B12 levels, both homocysteine and methylmalonic acid can be elevated – proving a functional deficiency of the nutrient. If only homocysteine is elevated, then a concomitant folate deficiency may also be present. These findings are due the fact that cobalamin (B12) is a cofactor in the conversion of homocysteine to methionine as well as methylmalonyl-CoA to succinyl-CoA. Folate is involved in the methylation of cobalamin to methylcobalamin that in turn methylates homocysteine to methionine. Folate is not involved in the conversion of methylmalonyl-CoA to succinyl-CoA.

Patients starting on ethambutol or isoniazid should receive a baseline initial screening ophthalmic evaluation including formal visual field testing, color vision, dilated fundoscopic exam, visual acuity, and other baseline screening modalities (e.g., optical coherence tomography (OCT) of the optic nerve). OCT analysis of the retinal nerve fiber layer of the optic disk in EMB toxic optic neuropathy may show nerve fiber layer thinning that can appear prior to obvious changes in appearance of the fundus. Although generally an acute toxicity, retinal examination of patients with methanol poisoning can show white striated edema of the peripapillary retina that eventually leads to bilateral and severe optic atrophy.

Patients with clinical symptoms consistent with a proven diagnosis of toxic/nutritional or hereditary optic neuropathy may still require further testing including a neuroimaging study and preferably magnetic resonance imaging (MRI) of the brain and orbit with and without contrast with fat saturation. Some patients with progressive unexplained optic neuropathy may need lumbar puncture and further evaluation for infectious, inflammatory, ischemic, infiltrative, or paraneoplastic etiologies. Leber hereditary optic neuropathy (LHON) mitochondrial DNA mutation testing and heavy metal screening could be considered even in patients with B12 or folate deficiency as some patients have multifactorial disease.

Differential Diagnosis

1. Compressive optic neuropathy/infiltrative optic neuropathy
2. Maculopathy/macular dystrophy
3. Bilateral inflammatory/infectious, e.g., syphilis
4. Bilateral demyelinating optic neuropathy
5. Radiation optic neuropathy

Therapy

The first step in the treatment of nutritional deficiency is vitamin replacement. In addition, the ophthalmologist should recommend discontinuation of smoking/alcohol use. When drug or substance toxicity is suspected, the offending agent (e.g., EMB) should be discontinued but only in consultation with the prescribing physician. Treatment should then depend on the cause of the disorder. Treatment for chemical-induced optic neuropathies includes correction of the concomitant acute systemic deficiencies and correction of electrolyte abnormalities including metabolic acidosis with administration of IV sodium bicarbonate. In methanol poisoning, ethanol can also be administered to compete with the metabolism of methanol into its more destructive and toxic by-products but has largely been supplanted by fomepizole. Hemodialysis is indicated if methanol is detected at blood levels over 50 mg/dL.

Treatment for isoniazid-induced optic neuropathy includes administration of pyridoxine 25–100 mg/day to help stabilize or possibly reverse the neuropathy and may occur independent of our simultaneously with EMB toxicity. Although there is no proven treatment for LHON, discontinuation of metabolic stressors (e.g., smoking and excessive alcohol use), vitamin supplementation, and perhaps treatment with coenzyme Q10 analogs may be helpful. A few clinical trials with idebenone have shown modest limited benefit but have been advocated by some authors.

Prognosis

Depending on the duration and severity of the findings, some cases of nutritional optic neuropathy have a favorable prognosis. However, permanent optic atrophy or temporal disk pallor can occur depending on the timing of diagnosis and start of treatment. Patients usually see improvement within 1–2 months of nutritional supplementation although in some individuals, improvement may not occur for 1 year.

Patients with EMB toxicity may still recover normal visual function after drug discontinuation. However, if significant optic disk pallor is already present, visual recovery is less likely to occur. Thus, early recognition and discontinuation of

the drug are critical before the development of irreversible optic atrophy.

There is currently no treatment for LHON; however, the prognosis of the disease can depend on the timing of diagnosis and the exact mutation of the gene. Patients with the 14484 mutation can have recovery of their vision but not until several months after the initial onset of vision loss. Patients with the 11778 mutation however have a much less favorable prognosis with over 75% becoming legally blind in both eyes.

Cross-References

- ▶ Demyelinating Optic Neuropathy
- ▶ Inflammatory Eye Disease
- ▶ Macular Dystrophy
- ▶ Optic Neuropathy

Further Reading

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T-PRK

- ▶ Transepithelial Photorefractive Keratectomy

Trachoma

- ▶ Chlamydia

Tractional Retinal Detachment

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Definition

Retinal detachment is, by definition, a condition in which subretinal fluid accumulates in the space between the neurosensory retina and the underlying retinal pigment epithelium (RPE), causing the separation of the two layers. There are different types of retinal detachment, depending on the mechanism of subretinal fluid accumulation. Tractional retinal detachment (TRD) is the second most common type after rhegmatogenous retinal detachment (RRD). A tractional retinal detachment occurs when scar tissue or other abnormal tissue grows, pulling the retina away from the layer beneath. Sometimes retinal tears can develop as a consequence of the mechanical traction on the retina, but they do not represent the leading cause for the detachment.

Etiology

The retinal surface can be considered a scaffold for abnormal tissue growth into the vitreous cavity in different pathological conditions. The strict connection existing between the inner retina and the abnormal intravitreal tissue, combined with a progressive contraction of the latter, generates an inward mechanical force responsible for the separation of the neurosensory retina from the underlying RPE.

Different pathologies can generate this condition, often as a late stage complication.

Proliferative vitreoretinopathy (PVR) is the clinical syndrome associated with retinal traction and detachment in which cells with proliferative potential multiply and contract on retinal surfaces and in the vitreous compartment. PVR presents with a spectrum of severity ranging from subtle retinal wrinkling, to fixed folds and tears with rolled edges, and to total rigid retinal detachment, retinal shortening, and advanced periretinal proliferation.

PVR is characterized by proliferation of cells derived from retinal pigment epithelium, glia, or inflammatory recruitment on the retinal surfaces and within the vitreous gel. These metaplastic cells transdifferentiate and assume contractile properties through internal cellular contractile proteins and by laying down extracellular collagen. They multiply and grow along available scaffolding, either the retinal surfaces or elements of residual vitreous gel. Mass contraction leads to retinal wrinkles, folds, tears, and traction retinal detachment.

PVR is the most common cause of failure in retinal detachment surgery. It can occur in untreated eyes with retinal detachment, especially with vitreous hemorrhage, or after cryotherapy or even laser retinopexy, pneumatic retinopexy, scleral buckling or vitrectomy, and after a variety of surgical complications. It is common after penetrating injuries and a variety of conditions associated with prolonged inflammation.

Proliferative diabetic retinopathy is characterized by new vessel formation, usually arising from retinal veins, that grows into the vitreous cavity. VEGF, overexpressed by the ischemic retina, is the main driver of the neovascularization process.

Once the stimulus for the growth of new vessels is present, the path of subsequent growth taken by neovascularization is along the route of least resistance.

Neovascularization seems to grow more easily on a preformed connective tissue framework. Thus, a shallowly detached posterior vitreous face is a frequent site of growth of new vessels. The new vessels usually progress through a stage of further proliferation, with associated connective tissue formation.

As PDR progresses, the fibrous component becomes more prominent, with the fibrotic tissue being either vascular or avascular. The fibrovascular variety usually is found in association with vessels that extend into the vitreous cavity or with abnormal new vessels on the surface of the retina or disc. The avascular variety usually results from organization or thickening of the posterior hyaloid face. Vitreous traction is transmitted to the retina along these proliferations and may lead to traction retinal detachment.

The same mechanism can explain a late onset of a tractional retinal detachment as a complication of other retinal vascular pathologies such as retinal vein occlusion, sickling hemoglobinopathies, and retinopathy of prematurity (ROP).

Clinical Presentation

Vitreoretinal traction develops insidiously in most cases.

The visual field defect progresses slowly and may become stationary for months or years.

If the macula becomes involved, the patient will experience a drop in vision.

The retinal detachment has a concave configuration, with the highest elevation of the retina occurring in the site of traction. Tractional retinal detachment is shallower than the rhegmatogenous one, and the retina appears to be more rigid. Usually retinal breaks are absent and, even if in some cases, isolated, or multiple retinal breaks can be detected.

Extensive PVR has fixed folds with retinal detachment especially inferiorly and fine membranes bridging the valleys between folds, as well as decreased mobility of the detached retina. Advanced PVR with posterior vitreous detachment results in the eventual formation of a funnel-shaped detachment with a contracted equatorial membrane.

In proliferative diabetic retinopathy, two types of retinal detachments occur: those that are caused by traction alone (nonrhegmatogenous) and those caused by retinal break formation (rhegmatogenous). Characteristics of nonrhegmatogenous

(traction) detachment in PDR include the following:

- The detached retina usually is confined to the posterior fundus and infrequently extends more than two thirds of the distance to the equator.
- The detached retina has a taut and shiny surface.
- The detached retina is concave toward the pupil.
- No shifting of subretinal fluid occurs.

Occasionally, a spontaneous decrease in the extent of a traction detachment may occur, but this is the exception rather than the rule. Traction on the retina also may cause focal areas of retinoschisis, which may be difficult to distinguish from full-thickness retinal detachment; in retinoschisis, the elevated layer is thinner and more translucent.

Diagnosis

Tractional retinal detachment has to be differentiated from other forms of retinal detachment:

- Rhegmatogenous retinal detachment
- Exudative retinal detachment

An accurate fundus evaluation can be enough to separate these conditions.

Since different retinal vascular disorders, all leading to a tractional retinal detachment as a late step of their natural history, are sometimes clinically difficult to differentiate, ancillary exams are advocated:

- B-scan ultrasonography
- Fluorescence angiography
- OCT

Differential Diagnosis

- Rhegmatogenous retinal detachment
- Exudative retinal detachment
- Proliferative vitreoretinopathy
- Proliferative diabetic retinopathy
- Retinal vein occlusion
- Eales disease
- Retinopathy, hemoglobinopathies
- Retinopathy of prematurity

Prophylaxis

Patients with retinal vascular disorders should be strictly monitored in order to assess the progression of the disease. If neovascularization develops, a complete pan-retinal photocoagulation has to be performed. Several studies have shown that laser photocoagulation of ischemic retina, prior to the development of new vessels, does not reduce the risk of neovascularization and further related complications.

In retinopathy of prematurity, a close follow-up is strongly indicated. Patients should be treated with photocoagulation as indicated.

Therapy

Surgical intervention is the only therapeutic modality for this ocular condition.

In case of tractional retinal detachment without retinal breaks, the main surgical goal is to relieve traction in order to let the neurosensory retina get in contact with the retinal pigment epithelium.

In those cases in which both a tractional and a rhegmatogenous component are detected, the purpose of the surgery is not only to relieve the traction but also to seal the breaks.

Pars plana vitrectomy represents the technique of choice.

A complete vitrectomy with epiretinal membrane peeling (with forceps and/or vitrectomy probes) is indicated in cases of severe PVR. Perfluorocarbon liquid can be used during the procedure, in order to stabilize the posterior retina. Care must be taken during epiretinal membrane dissection in order not to create iatrogenic retinal breaks. If traction is generated by a subretinal membrane, this can sometimes be removed by using a vitreoretinal forceps after a small

retinotomy has been created to give access to the subretinal space.

If residual traction remains, subretinal membranes may not be excised and a relaxing retinectomy can be created.

Pars plana vitrectomy is also indicated in case of severe diabetic retinopathy, late stages of retinal vein occlusion with neovascularization and retinal detachment, and retinopathy of prematurity.

Particular care must be taken during the fibrovascular membrane dissection not to generate intraoperative bleeding (endodiathermy of neovascular tissue) and/or retinal breaks.

Intravitreal bevacizumab has been reported as a preoperative adjunct in vitrectomy for PDR. Anti-VEGF drugs seem to reduce the bleeding associated with the segmentation and delamination of fibrovascular membranes. However, in eyes with severe ischemia, the neovascularization regresses rapidly, but the resulting fibrous scar tissue may lead to the development or progression of TRD.

Prognosis

Visual prognosis depends on the underlying cause of TRD. In case of a macular involved retinal detachment, prognosis is quite poor, even after the anatomical integrity of the eye has been restored (retinal reattachment rate 80–90%).

Epidemiology

PVR is responsible for most failures of retinal reattachment surgery. It occurs in about 7% of eyes after retinal reattachment surgery. In 1 year, approximately 1,600 new cases of PVR are seen.

Diabetic retinopathy is the leading cause of blindness in the working age group. In the 1960s, prior to the advent of laser photocoagulation, up to 50% of patients with PDR were legally blind. With new techniques, currently only 5% of patients with PDR progress to legal blindness.

A recent estimate of the overall incidence of ROP is 0.17%, but it is nearly 16% for premature infants.

Overall, 65.8% of infants developed some degree of ROP, and 6% reached threshold.

The median onset of stage 1 ROP was 34 weeks GA. The median onset of threshold disease was 37 weeks, with a range of 33.6–42 weeks GA.

Cross-References

- ▶ Neovascular Glaucoma in Proliferative Diabetic Retinopathy
- ▶ Pars Plana Vitrectomy
- ▶ Proliferative Endotheliopathy
- ▶ Retinopathy of Prematurity
- ▶ Optic Disc in Central Retinal Vein Occlusion
- ▶ Retinal Detachment Rhegmatogenous

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Tramacin

- ▶ Intravitreal Triamcinolone

Transcaruncular Route, for Anterior Orbitotomy

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Definition

A transconjunctival orbitotomy through the caruncle designed to access the medial orbital wall and extraperiosteal space.

Indications

This procedure is a very useful and direct approach to access the medial wall for medial wall decompressions, subperiosteal abscess drainage, or orbital fracture repair. This incision avoids skin incisions and vastly reduces the risk of visible scarring.

Contraindication

Contraindications for patients with any chronic or acute conjunctivitis or uncontrolled disease of the conjunctiva, such as ocular cicatricial pemphigoid. Also contraindicated in patients who are not medically stable for surgery (Cockerham et al. 2001; Nerad 2001; Levine 2003).

Techniques and Principles

In the operating room under sedation or general anesthesia, a Westcott scissors is used to make a vertical caruncular incision approximately in the middle of the caruncle. This may extend for approximately 10–15 mm and may be combined with an inferior transconjunctival incision for broader exposure. Blunt and sharp dissection is then carried out posteriorly and medially to avoid damage to the medial rectus until the area of interest is reached, usually the medial wall. At the end of the procedure, one or two chromic sutures may be used to close the caruncular incision (Cockerham et al. 2001; Nerad 2001; Levine 2003).

Outcome

Direct access to the medial wall with simple closure and minimal risk of scarring.

Complications

Risks include anesthesia, bleeding, pain, infection, scarring, swelling, loss of vision, damage to adjacent structures, diplopia, and need for additional procedures.

Cross-References

- ▶ Abscesses, Orbital
- ▶ Extraperiosteal Route
- ▶ Graves' Ophthalmopathy
- ▶ Ocular Cicatricial Pemphigoid (OCP)
- ▶ Orbital Hemorrhages
- ▶ Orbitotomy
- ▶ Transconjunctival Route

References

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Levine M (ed) (2003) Manual of oculoplastic surgery, 3rd edn. Elsevier Science, Philadelphia, pp 283–302

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Transconjunctival Route

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Definition

An anterior orbitotomy performed by creating incisions through the conjunctiva for access to a particular area, usually the inferior orbita or medial intraconal space.

Indications

To gain access to the orbit for optic nerve sheath fenestration medially or inferiorly for orbital fracture repair, decompression, abscess drainage, etc.

Contraindication

Lesion deeper in the orbit or not able to be accessed via anterior orbitotomy. Scarring diseases of the conjunctiva such as cicatricial pemphigoid. Any medical contraindication to surgery.

Techniques and Principles

A transconjunctival medial orbitotomy is performed with an incision made at the corneal limbus as a partial peritomy. The medial rectus can temporarily be disinserted from its origin for access to the medial intraorbital space (Fig. 1). This is often used for optic nerve fenestration or biopsy, or for medial rectus biopsy.

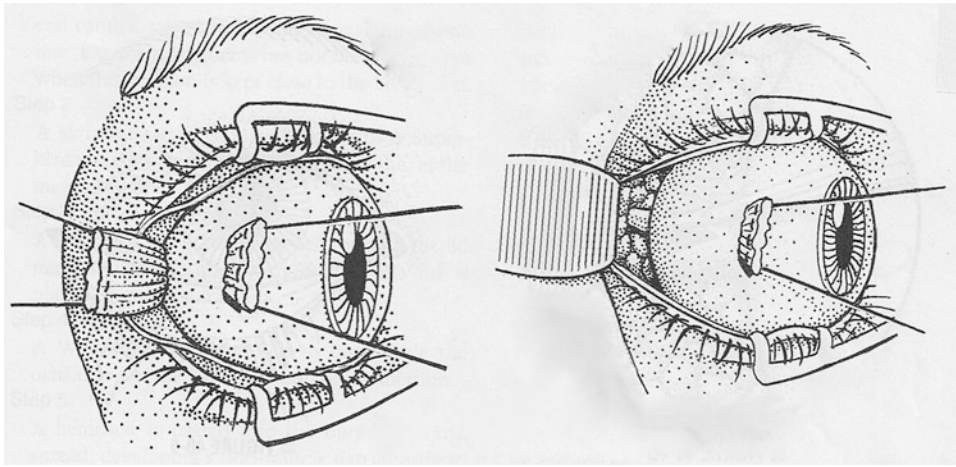
A transconjunctival lower eyelid orbitotomy is performed by an incision placed 1–2 mm beneath the inferior tarsal border dividing the retractors and the septum as necessary. The inferior extraconal space can be approached easily in this fashion without an external incision, eliminating the risk of potential scar. Furthermore, this approach may reduce the risk of lower eyelid retraction that may be more common with a transcutaneous, infraciliary incision. Furthermore, the transconjunctival incision can be combined with a lateral canthotomy and cantholysis for even broader access into the lateral orbit (Fig. 2) (Nerad 2001; Levine 2003).

Outcome

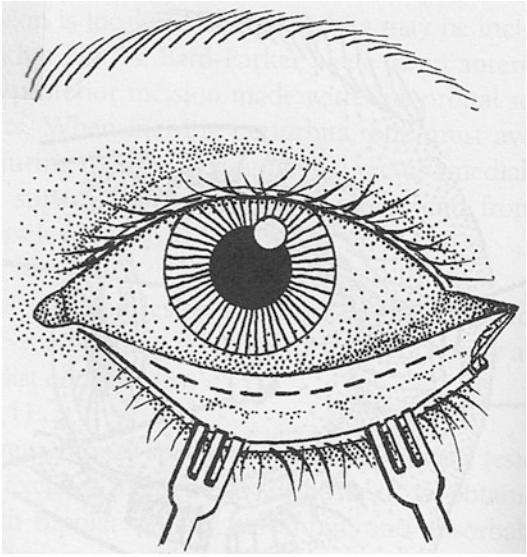
Allows exposure of the orbital contents while eliminating external incisions and therefore reducing risk of visible scarring.

Complications

Risks of the transconjunctival approach include risks associated with anesthesia, bleeding, pain, infection, scarring, swelling, loss of vision, damage to adjacent structures, diplopia, ptosis, eyelid retraction, cicatricial entropion, and need for additional procedures.



Transconjunctival Route, Fig. 1 The transconjunctival approach to the medial orbitotomy. A peritomy has been performed and the medial rectus identified and disinserted from the globe (*left*). A tag on the medial rectus insertion rotating the globe laterally and exposing the medial intraconal space and the optic nerve (*right*) (Printed with permission from Levine M, ed. Manual of Oculoplastic Surgery. 3rd ed. Philadelphia: Elsevier Science Inc., 2003: 291)



Transconjunctival Route, Fig. 2 The transconjunctival approach to the inferior orbit combined with a lateral canthotomy and cantholysis for broader exposure (Printed with permission from Levine M, ed. Manual of Oculoplastic Surgery. 3rd ed. Philadelphia: Elsevier Science Inc., 2003: 292)

Cross-References

- Abscesses, Orbital
- Anterior Orbitotomy
- Infraciliary Blepharoplasty Incision, for Anterior Orbitotomy
- Nasoethmoid Orbital Fractures
- Ocular Cicatricial Pemphigoid (OCP)
- Optic Disc (Optic Nerve Head)
- Orbital Hemorrhages
- Transcutaneous Routes
- Transseptal Route, for Anterior Orbitotomy

References

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Transcutaneous Routes

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Synonyms

Eyelid crease incision; Infraciliary incision; Subciliary incision

Definition

An orbitotomy, usually anteriorly, approached via a skin incision. This may be through the upper eyelid crease or infraciliary line. It allows access to a specific area of the anterior 2/3 of the orbit, generally.

Indications

To access an area of the orbit for biopsy of a lesion, removal of a lesion, removal of a foreign body, or for fat or bony orbital decompression. The goal is to provide the most direct route within incisions that follow natural skin lines and minimizing the risk of scarring.

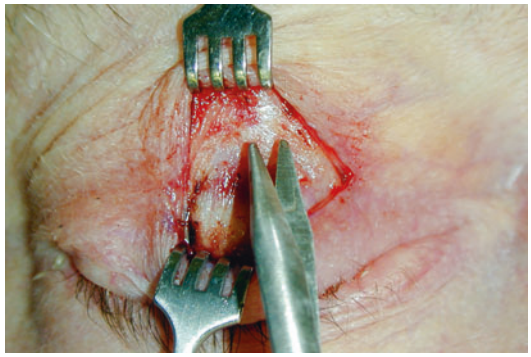
Contraindication

Lesion deeper in the orbit or not able to be accessed via anterior orbitotomy. Any medical contraindication to surgery.

Techniques and Principles

This procedure is generally performed in the operating room under sedation or general anesthesia. For superior lesions, an eyelid crease is marked (Fig. 1) and dissection is carried posteriorly

Transcutaneous Routes, Fig. 1 An eyelid crease incision is marked



Transcutaneous Routes, Fig. 2 Sharp and blunt dissection is carried out posteriorly. Here the Westcott scissors are aimed towards the septum for release and dissection in the transseptal plane

(Fig. 2), usually involving a transseptal incision to reach further back in the orbit or involving the lacrimal gland. More anterior lesions may not require opening of the septum. An inferior lesion may be approached via a transcutaneous incision in the subciliary area (Cockerham et al. 2001; Nerad 2001; Levine 2003).

Outcome

Allows for biopsy, lesion removal, foreign body removal, drainage of orbital abscess, and orbital decompression as necessary.

Complications

Risks of the transcutaneous approach include risks associated with anesthesia, bleeding, pain, infection, scarring, swelling, loss of vision, damage to adjacent structures, diplopia, ptosis, eyelid retraction, and need for additional procedures (Cockerham et al. 2001; Nerad 2001; Levine 2003).

Cross-References

- ▶ Anterior Orbitotomy
- ▶ Graves Ophthalmopathy
- ▶ Implants, Orbital
- ▶ Transconjunctival Route
- ▶ Transseptal Route, for Anterior Orbitotomy

References

Cockerham KP et al (2001) Surgery for orbital tumors. Part II: transorbital approaches. Neurosurg Focus 10:1–6

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Transepithelial Photorefractive Keratectomy

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Synonyms

T-PRK

Definition

Photorefractive keratectomy, in which the epithelial removal is performed by an excimer laser prior to stromal ablation.

Epidemiology

No epidemiological data available.

History

Transepithelial photorefractive keratectomy followed shortly after the first regular PRK was introduced in 1988.

Clinical Features

The corneal epithelium can be removed with a rotating brush, a surgical blade, an alcohol, or the excimer laser.

Please refer to the PRK section in this book for a detailed description of the PRK treatment and the features of the laser.

Tests

Thorough examination of the anterior segment with the slit lamp and corneal topography, pachymetry, and measurement of uncorrected and best spectacle-corrected visual acuity are mandatory to maintain best possible postoperative results.

Differential Diagnosis

Other types of surface ablation during PRK:

- PRK with alcohol, brush, and surgical blade

Etiology

See History section in the PRK chapter.

Treatment

After Bowman's layer is exposed, the excimer laser is focused on the surface in order to remove the right tissue. For myopic ablations, the central cornea is involved; for hyperopic ablations, the mid-periphery; and for astigmatic ablations, an area around the pupil. After the procedure, the surface is covered with a bandage contact lens, and postoperative medication is given.

Cross-References

▶ Femtosecond laser
▶ PRK
▶ wg-LASIK

Further Reading

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Transient Benign Unilateral Pupillary Dilation

▶ Benign Episodic Pupillary Mydriasis

Transient Cerebral Blindness

▶ Eclampsia, Neuro-Ophthalmic Disorders, Transient Visual Loss

Transient Cortical Blindness

▶ Eclampsia, Neuro-Ophthalmic Disorders, Transient Visual Loss

Transient Light-Sensitivity Syndrome

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Synonyms

Delayed acute photophobia; Good acuity plus photophobia; TLSS

Definition

An episode of acute photophobia after femtosecond laser LASIK in absence of other clinical signs and symptoms. The onset of TLSS is typically 2–4 weeks postoperatively (Stonecipher et al. 2006), and virtually no signs at the slit lamp have been described. In most cases, visual acuity is not affected. A good response to topical steroids suggests an inflammatory origin.

Higher laser energy settings (raster and side cut energy) in the early days of femtosecond laser LASIK were associated with the higher incidence of TLSS. A reduction of the laser energy led to significant decrease of TLSS incidence.

Histology

Anecdotal reports of confocal in vivo microscopy showed a higher prevalence of activated keratocytes at the flap stroma (Stonecipher et al. 2006).

Differential Diagnosis

Another condition that lead to photophobia after LASIK is, in particular, diffuse lamellar keratitis (DLK) (Linebarger et al. 2000). An increased incidence of DLK in eyes with TLSS has been reported. Other differential diagnoses are dry eye syndrome and infectious keratitis.

Cross-References

▶ Anterior Lamellar Keratoplasty (ALK)
▶ Femtosecond Laser
▶ Custom LASIK

References

Linebarger EJ, Hardten DR, Lindstrom RL (2000) Diffuse lamellar keratitis: diagnosis and management. J Cataract Refract Surg 26:1072–1077

Stonecipher KG, Dishler JG, Ignacio TS, Binder PS (2006) Transient light sensitivity after femtosecond laser flap creation: clinical findings and management. J Cataract Refract Surg 32:91–94

Transient Monocular Vision Loss (TMVL)

▶ Monocular Transient, Visual Loss Embolic Causes of
▶ Monocular Transient Visual Loss, Hypoperfusion Causing
▶ Monocular Transient Visual Loss in Carotid Artery Disease
▶ Monocular Transient Visual Loss, Ocular Causes of
▶ Monocular Transient Visual Loss, Orbital Causes of
▶ Monocular Transient Visual Loss, Stroke After
▶ Monocular Transient Visual Loss, Systemic Causes of

Transient Monocular Visual Loss

► Amaurosis Fugax

Transient Obscurations of Vision

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Synonyms

TVOs

Definition

Transient visual obscurations (TVOs) manifest as transient or brief darkening, blackening, or graying out of vision lasting seconds at a time. The episodes of typical TVOs are different in quality and duration than typical ischemia-related transient visual loss and are often described as fleeting and very short in duration (i.e., typically seconds). TVOs typically occur after bending over or altering head position. Disruption in axonal transport, the intracellular process through which axons are supplied with products synthesized in cell bodies, is thought to cause TVOs.

TVOs are commonly seen in patients with papilledema but may also occur in other optic nerve head disorders (e.g., pseudopapilledema). The short and diffuse nature of the episodes is more suggestive of TVO as compared with ischemic amaurosis fugax episodes from hypotension, hypoperfusion, thrombosis, or embolic disease.

Cross-References

► Idiopathic Intracranial Hypertension

Further Reading

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Transplantation

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Synonyms

CLAL; CLAU; DALK; DLEK; DMEK; DSAEK; DSEK; KLAL; PK; Scleral patch graft, corneal patch graft

Definition

An operation moving an organ from a donor to the recipient. The donor tissue may consist of cornea, conjunctiva, or amniotic membrane and can be either an allograft or an autograft.

Indication

Corneal pathology such as visually significant scarring, ectatic disease, and Fuchs dystrophy are all surgical indications for a lamellar or penetrating keratoplasty. In cases of partial or total limbal stem-cell deficiency, pterygia, or symblepharon, conjunctival or amniotic membrane transplantation can be done.

Contraindication

Poor surgical candidates from a systemic standpoint and operating on an NLP eye (unless there is psychological contraindication to enucleation or evisceration) would be absolute contraindications. Relative contraindications include ocular surface disorders like uncontrolled dry eye and meibomian gland disease, trichiasis, entropion and ectropion, lagophthalmos, limbal stem-cell deficiency, neurotrophic disease, and pemphigoid (Brightbill et al. 2009).

Techniques and Principles

When an allograft is transplanted, the donor tissue is recognized by the recipient's immune system. This activation can result in formation of specific antibodies and lymphocytes directed toward the donor tissue, resulting in rejection. Typically, the cellular antigens that cause this response are human leukocyte antigens (HLA). HLA matching between donor and recipient is common in most organ transplants, but for corneal transplants, studies such as the collaborative cornea transplantation study (CCTS) showed no benefit to HLA matching. The CCTS also found that ABO-compatible corneas showed no benefit in rejection rates as compared to ABO-incompatible corneas, though there was a higher failure rate in the incompatible group (The Collaborative Corneal Transplantation Studies (CCTS) 1992). The reasons for this include a lack of vascularization in the normal cornea with associated "immune privilege," anterior chamber-associated immune deviation (ACAID), and a lack of antigen-presenting (Langerhans) cells in the central cornea (Krachmer et al. 2005). Typically, rejection can be avoided with topical steroids.

For conjunctival and scleral allografts, vascularization at the site of transplantation can cause a more pronounced immune response. As a result, living-related donors are preferable if an autograft is not possible. HLA matching and ABO typing can even be used to find the best familial match. For surgeries such as KLALs or high-risk corneal transplants, oral immunosuppressive agents may be required.

Tissue is procured from organ donors and processed at eye banks throughout the world. Typically, the death to preservation time is about 6 h, and the tissue can be stored in different storage media which allow a window for the tissue to be used without fear of oxidative damage or contamination. This time period is approximately 7–10 days in the United States and approximately 4 weeks in Europe. Hypothermic storage is typically used (Armitage 2011).

Techniques specific to each procedure can be found in the appropriate cross-referenced article.

Outcome

Outcomes vary depending on the particular transplant being performed and the risk factors.

Complications

Infection, hemorrhage, graft rejection, wound dehiscence, expulsion of intraocular contents, glaucoma, retinal detachment, cataract, and risks of general anesthesia.

Cross-References

- ▶ Amniotic Membrane Transplantation Nonpharmacotherapy
- ▶ Conjunctival Autograft

- ▶ Deep Anterior Lamellar Keratoplasty (DALK)
- ▶ Deep Lamellar Endothelial Keratoplasty (DLEK)
- ▶ Keratoprosthesis
- ▶ Limbal Autograft/Allograft (Limbal Transplantation)
- ▶ Primary Endothelial Failure, After Penetrating Keratoplasty
- ▶ Tectonic Penetrating Keratoplasty, for Herpetic Keratitis

References

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Transplantation, Amniotic Membrane

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Synonyms

Amnion

Definition

Amniotic membrane is the innermost layer of the placenta that lines the amniotic cavity. It contains a thick basement membrane that provides nourishment and encourages epithelial cell growth. The avascular stromal matrix suppresses TGF-beta and proliferation of fibroblasts, thereby decreasing scarring. The tissue is harvested from pregnant mothers undergoing caesarian section. These women are screened for HIV, hepatitis B and C, and syphilis to ensure healthy tissue (Krachmer et al. 2005). The tissue is harvested, washed in BSS, soaked in antimicrobial solution for 24 h, and then rewashed in BSS. The amniotic membrane is stripped from the chorion, placed on nitrocellulose strips, cut into small pieces, and frozen at −80 °C. Besides the wet form of AMT, the tissue can be dehydrated after being stripped from the chorion. Many surgeons feel this dehydrated form is easier to handle intraoperatively. Because of some concerns about the true sterility of the amniotic membrane harvest process, a freeze-dried dehydrated amniotic membrane is also available. This tissue is similarly procured, but is exposed to gamma radiation, effectively denuding the tissue (Nakamura et al. 2004).

Indication

Because of its efficacy is promoting healing, it has been used as a graft for conjunctival disorders such as conjunctivochalasis, symblepharon, pterygium, bleb leaks, scleral melts, and lid and orbit reconstruction. It can also be used as a graft for corneal disorders such as partial limbal stem cell deficiency, persistent corneal defects, chemical burns, band keratopathy, and bullous keratopathy. Amniotic membrane can also be used as a patch for Stevens-Johnson syndrome, preventing scars after PRK or PTK or for persistent keratitis recalcitrant to other treatment (Tseng 2001).

Contraindication

Amniotic membrane transplantation (AMT) only helps promote healing, so it requires the host

tissue to supply epithelial and mesenchymal cells. Total limbal stem cell deficiency, severe aqueous tear deficiency, severe neurotrophic state, stromal ischemia, and diffuse keratinization are contraindications.

Techniques and Principles

Once an area to be treated with AMT has been defined, it is important to first achieve meticulous hemostasis. The defect must then be measured. The amniotic membrane comes in a sterile pouch, which can be opened and removed using non-toothed forceps. The membrane can be cut to the desired size. Some surgeons prefer to cut a size slightly larger than the measured defect. To help with orientation, amniotic membrane comes with a watermark on the tissue. When the series of letters is read appropriately, the surgeon knows that the tissue is oriented with the stromal side down. This is the most popular orientation, though it is debatable. If the membrane is dehydrated, a few seconds of lubrication will cause the tissue to swell, which eases the manipulation. The tissue can be adhered to the eye by fibrin glue or by permanent or dissolvable sutures. Again, non-toothed forceps are recommended, as toothed forceps can macerate the tissue. If fibrin glue is used, it is important to remove any excess glue and to ensure that there are no adhesions to the lid speculum. Otherwise, removing the lid speculum at the end of the case could result in accidental removal of the membrane. An AMT done in this fashion is typically done in the OR. To facilitate clinical use for nonhealing epithelial defects, an amniotic membrane with a thermoplastic ring set (Prokera) can be applied similar to a large contact lens.

Outcome

The membrane often dissolves in 1–2 weeks, expediting epithelial healing and preventing scarring.

Complications

Infection, hemorrhage, early disintegration and dehiscence, and no beneficial effect have all been reported.

Cross-References

- ▶ Amniotic Membrane Transplantation Nonpharmacotherapy
- ▶ Pterygium
- ▶ Stevens Johnson Syndrome
- ▶ Tissue Adhesives, Cyanoacrylate, for Anterior Segment

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Transposition Flap

- ▶ Z-Plasties

Transposition Flaps, for Lateral Canthal Defects

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Synonyms

Bilobed flap; Local advancement flap; Rhombic transposition flap; Z plasty

Definition

Transposition flaps are defined as local flaps, which are transposed from one area to another, usually over an intervening segment of normal tissue. Classic transposition flaps include rhombic transposition flaps, bilobed flaps, and z-plasty.

Indication

In the lateral canthus, transposition flaps are indicated for the repair of anterior lamellar (skin and muscle) deficiencies in which there is inadequate tissue available for direct simple closure. These defects are most commonly secondary to cancer resection surgery, including Mohs surgery, and trauma.

Contraindications

In trauma patients, eyelid surgery should be deferred until the patient is stable and a suitable candidate. Also more serious injuries, such as a ruptured globe, take precedence and should be repaired prior to the eyelids. The donor tissue to be transposed must be healthy and viable. Injury to the lateral canthal tendon should be assessed and surgically repaired if present.

Techniques and Principles

In designing an appropriate transpositional flap, the surgeon must carefully select the most favorable flap design for a given defect while considering local skin mobility. In general tissue, it is transposed from an area of relative excess to an area with insufficient tissue to allow closure. The orientation of relaxed skin tension lines can help in choosing the transposition flap design which will result in the least conspicuous scar.

A transposition flap from the upper eyelid based laterally can be transposed to fill a lateral canthal and partial lower eyelid defect. If the lateral canthal defect is large and involves the thicker skin of the upper cheek, a transposition flap from the area just superior to the eyebrow can be developed and rotated in position.

The rhombic flap is commonly utilized for reconstruction of lateral canthal defects owing to the presence of mobile tissue lateral to the lateral canthus and the ability to camouflage the acute angles which result from the repair in the lateral canthal rhytids. The defect is converted into a rhombus, which is defined as an equilateral parallelogram. In the classic rhombic flap, the angels of this parallelogram are opposing 60° and 120° angles. A line, equal in length to the short diagonal, is then extended as a continuation of the short diagonal. A line parallel to and equal in length to a side of the parallelogram is then extended from the tip of this previously drawn line. The lines are incised with a scalpel and the flap is undermined to the layer of the subcutaneous tissue plane then rotated and advanced to fill the skin defect.

A bilobed flap is a double transposition flap in which two successively smaller lobular shaped flaps are transposed to fill a single, often circular, defect. The bilobed flap is less useful in the lateral canthus because the geometry of the curved scars which result is often more conspicuous than the acutely angled linear scars which result from the use of rhombic transposition flaps.

Z plasty is a modified transposition flap and can be adapted for use in the lateral canthus as well.

Outcome

Transposition flaps allow for recruitment of anterior lamellar tissues (skin and muscle) for reconstruction of lateral canthal defects. The desired outcome is a functional lateral canthus which provides adequate support for normal eyelid function.

Complications

Any excess tension on the flap can result in wound dehiscence or flap necrosis. Phimosis and rounding of the lateral canthus can occur with healing, particularly if the lateral canthal tendon has been violated. Damage to the zygomatic branch of the facial nerve, with resultant

orbicularis occuli weakness, can occur with dissection in the lateral canthal region.

Cross-References

- ▶ Canthal Reconstruction
- ▶ Cantholysis
- ▶ Canthotomy
- ▶ Eyelid Reconstruction
- ▶ Horizontal Eyelid Shortening
- ▶ Rotational Flap for Eyelid Repair
- ▶ Semicircular Flap
- ▶ Tarsorrhaphy
- ▶ Tenzel Flaps
- ▶ Z-Plasties

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Transscleral Fixation

- ▶ Scleral Fixation of Intraocular Lens

Transseptal Route, for Anterior Orbitotomy

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Synonyms

Postseptal incision

Definition

An orbitotomy, usually anteriorly, approached via a transcutaneous (upper eyelid) or transconjunctival (lower eyelid) incision involving opening of the septum. This allows access to a specific area of the anterior 2/3 of the orbit, generally.

Indications

To access an area of the orbit for biopsy of a lesion, removal of a lesion, removal of a foreign body, or for fat or bony orbital decompression. The goal is to provide the most direct route within incisions that follow natural skin lines and minimizing the risk of scarring. The septum is released to allow more posterior exposure of the orbit (Cockerham et al. 2001; Nerad 2001; Levine 2003).

Contraindication

Lesion deeper in the orbit or not able to be accessed via anterior orbitotomy. Any medical contraindication to surgery.

Techniques and Principles

This procedure is generally performed in the operating room under sedation or general anesthesia. For superior lesions, an eyelid crease is marked and dissection is carried posteriorly. The septum is released and dissection is carried posteriorly or medially into the orbit. This allows access to the optic nerve for optic nerve fenestration, and any lesion in the anterior orbit for biopsy or removal. An inferior lesion may be approached via a transcutaneous incision in the

infraciliary area. The septum is released allowing prolapse of the fat and access to anterior lesions. This also allows fatty decompression in Graves' Ophthalmopathy (Cockerham et al. 2001; Nerad 2001; Levine 2003).

Outcome

Allows for biopsy, lesion removal, foreign body removal, drainage of orbital abscess, and orbital decompression as necessary.

Complications

Risks of the transseptal approach include risks associated with anesthesia, bleeding, pain, infection, scarring, swelling, loss of vision, damage to adjacent structures, diplopia, ptosis, eyelid retraction, and need for additional procedures.

Cross-References

- ▶ Anterior Orbitotomy
- ▶ Graves Ophthalmopathy
- ▶ Orbital Cellulitis
- ▶ Transconjunctival Route
- ▶ Transcutaneous Routes

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Transverse (Lateral) Sinus Thrombosis

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Definition

The intracranial lateral (transverse) venous sinuses (right and left) drain venous blood from the confluence of sinuses to the sigmoid sinuses. Thrombosis of the transverse (lateral) sinus can lead to reduced drainage of venous blood and secondary reduction in absorption of cerebrospinal fluid. As a result, transverse sinus thrombosis can lead to increased intracranial pressure (ICP), venous hypertension, or secondary hydrocephalus.

Symptoms of transverse sinus thrombosis can develop acutely and may mimic idiopathic intracranial hypertension (IIH). Typical symptoms of increased ICP include headache, diplopia associated with cranial nerve (CN) VI palsy,

papilledema, nausea, and vomiting. Furthermore, patients might also exhibit CN VII or CN VIII dysfunction.

Cross-References

► Idiopathic Intracranial Hypertension

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Transverse Chromatic Aberration

► Chromatic Aberration: Definition

Transverse Keratotomy

► Astigmatic Keratotomy

Transverse Tarsotomy

► Wies Repair

Transverse Tarsotomy Procedure

► Tarsotomy

Transverse Tarsotomy with Lid Margin Rotation

► Tarsal Fracture Operation, for Cicatricial Entropion

Trapezoidal Keratotomy

► Astigmatic Keratotomy

Trauma, Canalicular

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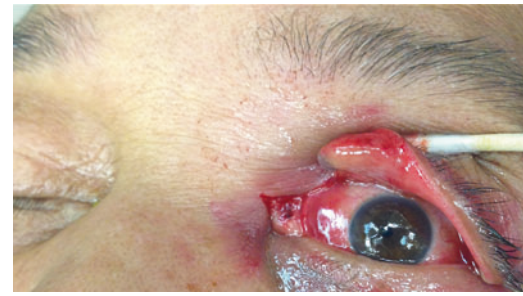
Definition

Trauma of the eyelid that involves the canalicular system.

Etiology

Blunt or penetrating trauma to the eyelid, orbit, or midface can cause injury to the canalicular system. The canalicular portion of the eyelid is weak and tears easily with forceful, laterally directed traction. Medial upper or lower eyelid lacerations are a common cause of canalicular trauma. Canalicular system damage can occur in association with medial canthal degloving injury due to anatomic proximity (Figs. 1 and 2).



Trauma, Canalicular, Fig. 1 Left upper lower lid eyelid injury with medial canthal involvement

Trauma, Canalicular, Fig. 2 Right upper eyelid laceration with medial canthal involvement secondary to strike with a fist

Clinical Presentation

With any acute injury to the medial portion of the eyelid, particularly lacerations or avulsion, canalicular trauma must be suspected. More remote injuries may present with chronic epiphora.

Diagnostics

The primary objective following orbital trauma is to evaluate and treat any sight-threatening injuries. Ruling out a ruptured globe is essential as manipulation of the eyelids to examine a laceration can cause expulsion of intraocular contents. Attention can then be directed to the eyelid and canalicular system.

Visual inspection is first performed to assess the nature and extent of injury. If canalicular damage is suspected, probing or irrigation of the canalicular system can demonstrate if the integrity of the lacrimal system has been compromised. Irrigation leaking through the wound site or flowing retrograde through the punctum indicates a canalicular laceration. When the Bowman probe is passed through the punctum, the wound is examined to determine if the tip is present. Eyelid trauma in children may require examination under anesthesia to fully evaluate extent of injury.

CT can be used to evaluate for presence of foreign body. MRI should be avoided with any concern for metallic foreign body. Naso-orbital-ethmoid (NOE) fractures often accompany damage to the lacrimal system.

Differential Diagnosis

Injury to the medial eyelid without damage to the canalicular system

Dacryocystitis

Canaliculitis

Prophylaxis

Safety eyewear

Therapy

Surgical reconstruction of the canalicular system at the time of primary eyelid repair is recommended to prevent chronic epiphora. Surgical repair should be undertaken within 24 h of the injury to prevent fibrosis and scarring. Surgical reconstruction can performed in the operating room under general anesthesia or with local anesthesia in a cooperative patient. Regardless of systemic anesthesia type, the area is locally anesthetized using lidocaine with epinephrine to minimize hematoma formation. Visual inspection of the injury is first performed, as the injury can be much larger than is evident on initial clinical exam. Debridement with copious irrigation removes foreign material. The upper and lower canalicular systems are dilated using Bowman probes to confirm the damaged canalicular system and to identify the cut end of the system. The alternate end of the canalicular system in the lacrimal sac is identified, and a silicone stent is

passed through the lacerated system into the distal system, through the lacrimal sac and into the nose. The silicone stents are typically left in place for weeks to months and then removed in the office.

Tetanus booster and systemic antibiotics may be recommended depended on the nature of the injury.

Prognosis

If stenting of the canalicular system is performed successfully, the prognosis is good. Not surprisingly, chronic epiphora is more common with combined upper and lower canalicular injuries. If repair is delayed, scarring of canalicular system can make intubation with stents more challenging.

Epidemiology

Canalicular trauma occurs most commonly in young adult males. Strike from a fist is the most common cause of canalicular laceration overall. Dog bits are the most common cause in children.

Cross-References

► Eyelid Trauma
► Silicone Intubation

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Trauma, Lacrimal Sac and Nasolacrimal Duct

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Definition

Trauma of the lacrimal sac and nasolacrimal duct.

Etiology

Etiology of lacrimal sac and nasolacrimal duct trauma is typically mechanical – be it penetrating laceration, avulsion, or blunt injury. High impact blunt trauma causing naso-orbital-ethmoid (NOE), Le Fort II, and Le Fort III type fractures are often associated with osseous or soft tissue injuries to the lacrimal sac and nasolacrimal duct. In 7–15% of all facial traumas, bony fractures of the nasolacrimal duct are discovered. Injury to the nasolacrimal system may be structural at the time of initial trauma or may develop from fibrosis and subsequent dacryostenosis. Iatrogenic causes of trauma to the lacrimal sac and nasolacrimal duct include probing, lacrimal intubation, and sinus surgery.

Clinical Presentation

Lacerations to the medial portion of the eyelid can be associated with soft tissue injury to the lacrimal sac. Patients may not develop tearing immediately and dacryocystitis or nasolacrimal duct

obstruction (NLDO) can be delayed complications caused by progressive fibrosis. Patients present to the ophthalmologist with symptoms of epiphora, mucopurulent discharge from the puncta, pain over the lacrimal sac, cellulitis, and dacryocystitis. Unilateral tearing suggests functional blockage as tearing from keratopathy typically results in symmetric hypersecretion. Whenever a patient presents with complaint of tearing, history taking should elicit remote history of facial trauma.

Diagnostics

Prior to evaluation of lacrimal system injuries, the patient should be stabilized from a medical perspective and examined for a ruptured globe. Trauma to the midface or medial eyelids, and/or CT scan demonstrating lacrimal fossa fracture, NOE fracture, or Le Fort II or III fractures raises suspicion for lacrimal sac or nasolacrimal duct injury. Thin volumetric CT imaging through the lacrimal sac fossa down through the inferior turbinate can be obtained with multiplanar and three-dimensional volume rendered reconstructions. MRI may be contraindicated if there is the potential for an occult metallic foreign body.

Irrigation of the lacrimal system demonstrates intact function of the tear drainage system when fluorescein is observed at the inferior turbinate or passes easily into the nasopharynx. With severe midface trauma, patent irrigation alone is not sufficient to rule out injury to the lacrimal sac or nasolacrimal passage as fluid may extravasate into the nose through a site of bony injury. Probing with a Bowman probe can more definitely assess the patency of the system in this setting. The distance and site of blockage in the upper system can be measured directly as the Bowman probe is held or marked at the site of obstruction. Observation of elevated tear lake and the dye disappearance test are not helpful in the setting of trauma due to high false positive rate.

With complaint of tearing in the outpatient setting, full history and ophthalmic exam must be undertaken to rule out hypereflexive or alternative etiologies of epiphora. History taking should include question of prior sinus surgery, facial trauma, radiation history, blood in tears, and medications. Full anterior segment examination with focus on lid position, puncta, and lacrimal sac should be performed. Palpation of the lacrimal sac revealing mucopurulent discharge indicates a patent common canaliculus and valve of Rosenmüller. Dye disappearance test is often the initial test performed to confirm a blocked tear nasolacrimal system. One drop of fluorescein dye into the fornix and, after 5 min, greater presence of dye in the fornix of the affected eye compared to the normal side suggests impaired drainage. The Jones I test can be performed simultaneously after the fluorescein is given. In the Jones I test, a cotton tip applicator is placed at the inferior turbinate at 2 and 5 min. If fluorescein is present on the cotton tip, the system is patent. This test is limited by a high false negative rate.

With a negative Jones I test, the Jones II test can more accurately identify the site and extent (complete/partial) of obstruction. Clear saline is flushed through the lacrimal sac using an irrigating cannula through the canaliculus. After forceful irrigation is performed, the patient is asked to spit or blow their nose into a tissue. Recovery of any fluid indicates a partial rather than complete blockage. Recovery of fluorescein indicates that the punctal and cananilcular anatomy are patent, as dye has accumulated in the lacrimal sac. A partial blockage is presumed to be in the lower system, either at the entry of the lacrimal sac to the nose or in the duct. If clear saline is recovered, a stenotic punctum or canalicular blockage is implicated as the fluorescein from the Jones I test never penetrated the lacrimal sac. Regurgitation of fluorescein from the upper lid puncta indicates complete blockage at the lacrimal sac. Regurgitation of clear saline from the upper lid puncta indicates obstruction at the common canaliculus. Palpation of the lacrimal sac also provides diagnostic utility. If the sac dilates during

irrigation, but no fluid passes into the nasopharynx, obstruction of the lower system is suggested. If there is sac fibrosis or scarring, the lacirmal sac may not dilate during irrigation.

Contrast dacryocystogram (DCG), CT dacryocystography, or MRI with topical Gadolinium has been used to image the nasolacrimal system. DCG is helpful for locating the site of anatomic obstruction but does not show any detail regarding surrounding soft tissue. Radionucleotide dacryoscintigraphy is less practical for identifying site of obstruction but provides information of physiologic functioning. Nasal endoscopy can be helpful to examine for nasal tumors, rhinitis, or nasal polyps causing blockade of the distal end of the nasolacrimal duct.

Differential Diagnosis

Eyelid malposition
Dacryocystitis
Other cause of acquired nasolacrimal duct obstruction
Primary acquired nasolacrimal duct obstruction
Hypersecretion of tears.

Prophylaxis

Safety eyewear.

Therapy

Tetanus booster and systemic antibiotics may be recommended depending on the nature of the injury.

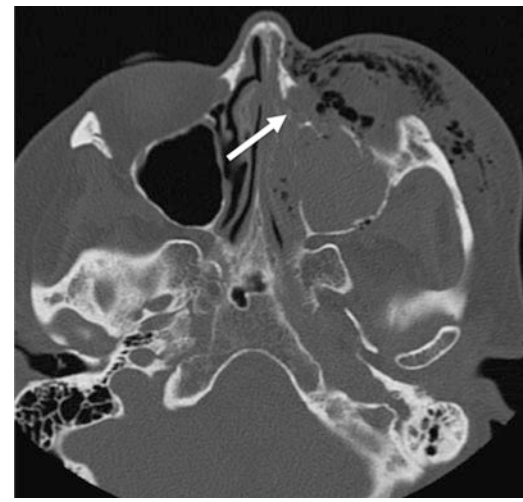
Repair of soft tissue damage in the context of the initial trauma is not usually possible. If the trauma is severe, with gross obstruction of the nasolacrimal system or displacement of bony anatomy, bicanalicular stents can be placed prophylactically. Midface reconstruction or plating of facial fractures can be performed in concurrence with or following silicone intubation with minimal disruption. The silicone tubes are then left in place for 3–6 months as is standard and can be removed in the office. With minimal damage, but suspicion of NLDO, dacryocystorhinostomy (DCR) or conjunctivo-DCR (C-DCR) can be performed at a later date. Symptoms of epiphora can also resolve over time as swelling in the system resolves, relieving transient blockage.

Prognosis

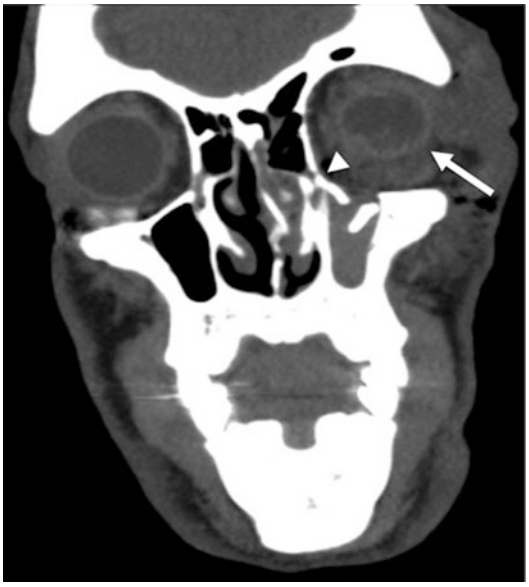
Success rate for surgical correction of epiphora related to NLDO is surprisingly high. DCR has demonstrated success in 92–100% of patients with NLDO following NOE fracture. Reports indicate that primary repair of midfacial fractures within 2 weeks of injury, typically by wide open reduction and fixation, reduces the incidence of NLDO following injury.

Epidemiology

Fractures of the nasolacrimal duct are reported in 7–15% of all facial traumas. NLDO following NOE fracture ranges in incidence from 29–68%.



Trauma, Lacrimal Sac and Nasolacrimal Duct, Fig. 1 Axial CT image in bone windows demonstrates a complex facial fracture with extension through the lacrimal bone and nasolacrimal duct (*arrow*), causing expansion of the lacrimal sac



Trauma, Lacrimal Sac and Nasolacrimal Duct, Fig. 2 Coronal CT in soft tissue algorithm demonstrates a comminuted fracture through the anterior orbital rim with a bony fragment (*black arrow*) disrupting the nasolacrimal duct following trauma caused by a blow to the orbit with a baseball bat. Also seen in this image is a globe rupture (*white arrow*) and extensive soft tissue hemorrhage, edema, and subcutaneous emphysema. Clinical exam revealed lacrimal system involving lower eyelid laceration

In one study, 17% of patients went on to DCR following severe naso-orbito-ethmoid injury.

Injuries are more common in young adult males. Mechanism of injury varies but most often includes fist, motor-vehicle accident, or animal associated injury (Figs. 1 and 2).

Cross-References

- ▶ Silicone Intubation
- ▶ Trauma, Canalicular
- ▶ Eyelid Trauma

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Traumatic Aniridia

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Synonyms

Iris deficiency; Iris prolapse

Definition

Traumatic aniridia is an anatomical condition in the eye that occurs after surgical or boisterous traumatic affection of the bulbus. This anatomical condition implicates a complete or incomplete destruction of the iris tissue with complete or incomplete tear of iris tissue from the iris base.

Histology

Immunohistochemistry
Electron microscopy
Molecular diagnostics

There are no data available in this topic.

Differential Diagnosis

– Iris coloboma and infantile aniridia

Further Reading

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Traumatic Glaucoma

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Synonyms

Acute contusion glaucoma

Definition

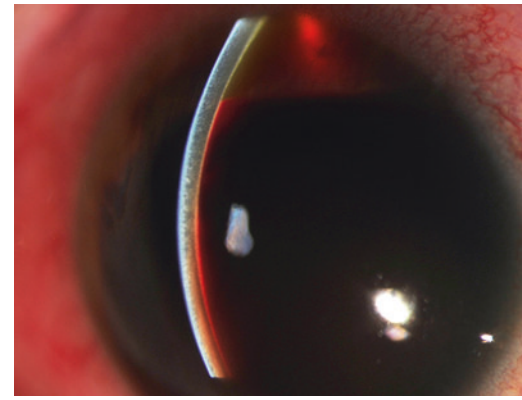
Trauma can cause IOP elevation by inflammation, red blood cells (hyphema), or direct injury of the trabecular meshwork or the lens with lens (sub) luxation (De Leon-Ortega and Girkin 2002). Each of these or a combination of them can be the reason for traumatic glaucoma. Normally, the IOP elevation is of short duration but could be prolonged with a risk of nerve damage (Herschler and Cobo 1982).

Etiology

Ocular trauma is the reason for the development of traumatic glaucoma.

Clinical Presentation

Hyphema (Fig. 1) often with rebleeding during the first week may cause IOP elevation by obstruction of the trabecular meshwork. The risk of elevated IOP increases by the amount of hyphema. On the other hand, a small hyphema can also cause a marked IOP raise, especially in an additionally and otherwise compromised angle (Schlote and Rohrbach 2005).



Traumatic Glaucoma, Fig. 1 Traumatic Glaucoma with Hyphema and Hematocornea

A posttraumatic inflammation may also lead to traumatic glaucoma caused by the same pathophysiologic mechanism, namely, the obstruction of trabecular meshwork by inflammatory cells, fibrin, and debris.

Direct injury of the trabecular meshwork may cause both hypertony and hypotony of the eye.

Diagnosis

Anamnesis and biomicroscopy.

Therapy

Local antiglaucomatous drugs are useful as a first-line therapy regimen supplemented by anti-inflammatory drugs (NSAR and corticosteroids) (Stamper et al. 2009).

Prognosis

Often depends on the underlying injury of the eye.

Epidemiology

Depends on the population.

Cross-References

- ▶ Angle Recession Glaucoma
- ▶ Eyelid Inflammation
- ▶ Hematoma
- ▶ Hyperopia
- ▶ Open-Angle Glaucomas

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Traumatic Iris Loss

- ▶ Aniridia, Traumatic

Traumatic Retinopathy

- ▶ Commotio Retinae (Berlin Disease/Edema)

Treacher Collins Syndrome

- ▶ Treacher Collins-Franceschetti Syndrome (Mandibulofacial Dysostosis)

Treacher Collins-Franceschetti Syndrome (Mandibulofacial Dysostosis)

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Synonyms

Franceschetti-Zwahlen-Klein syndrome; Mandibulofacial dysostosis; Treacher Collins syndrome

Definition

Treacher Collins-Franceschetti syndrome (TCFS) was first described in 1900 and is an autosomal dominant condition that is characterized by general craniofacial soft tissue and skeletal hypoplasia of the first and second branchial arches, with a wide spectrum of deformities.

Etiology

The disorder is caused by a mutation in the TCOF gene on chromosome 5q32-33.1, which encodes the treacle protein. Deletions in this gene cause haploinsufficiency in an autosomal dominant genotype, with deficiencies in ribosomal DNA transcription causing increased apoptosis of neural crest cells.

Clinical Presentation

The primary feature of TCFS is mandibular retrognathia, soft and hard tissue malar deficiency, downward-slanting palpebral fissures, euryblepharon with or without coloboma, and conductive hearing loss. The orbital region is

characterized by hypoplasia of the superior and inferior orbital rims, along with hypoplasia of the zygomatic bone. This creates the appearance of protruding globes, which along with euryblepharon of the lower lids, can predispose patients to development of exposure keratopathy. The orbicularis oculi muscles and meibomian glands along eyelid margins can be attenuated or absent, which can give the eyelid significant laxity. The absence of lashes in the medial third of the lower lid is a pathognomonic finding. Strabismus and congenital cataracts have been reported, and amblyopia can also result from corneal scarring.

Diagnosis

Prenatal ultrasound has been used for diagnosis of Treacher Collins, usually after 30 weeks of gestational age when most facial structures are visible, although most cases are diagnosed readily at birth through recognition of its clinical and radiographic features. The disorder can be diagnosed through mutations in the TCOF gene, although commercial assays are not available at the time of this publication.

Differential Diagnosis

Mandibulofacial dysostosis with microcephaly, Nager syndrome, Miller syndrome, Genee-Wiedemann syndrome.

Prophylaxis

There is no prophylaxis available for this genetic craniofacial condition. Infants should receive an ophthalmologic examination within 3 months of birth. Several interventions can be undertaken to prevent the development of exposure keratopathy, including lateral tarsorrhaphy or lower lid skin grafts. However, lower eyelid grafting is preferably deferred until later childhood when there is sufficient upper eyelid tissue available for grafting in order to address the lid coloboma.

Therapy

Interventions for TCFS require a multidisciplinary approach between ophthalmology and otolaryngology, plastic surgery, craniofacial specialists, pediatrics, orthodontics, speech and language pathology, and psychology. Starting at birth, there should be an airway evaluation, as well as monitoring of feeding progress. An ophthalmologist should evaluate the condition of the cornea within the first 3 months to determine whether any intervention is warranted at that point. CT imaging should be performed within the first 6 months in order to identify the cause of hearing loss, as mild cases with only ossicular discontinuity may be responsive to banded hearing aids and, after age 4, bone-anchored hearing aids. Eyelid reconstruction can be performed later in childhood when there is adequate tissue available for grafting. Distraction of the mandibular angle is performed later in childhood, followed by orthognathic surgery.

Prognosis

Through proper management, involvement of multidisciplinary teams, and appropriate intervention at various stages, reconstructive treatment and addressing hearing and vision issues can help patients lead productive lives, especially given that most patients with TCFS do not have neurodevelopmental impairment. As far as vision is concerned, early examination within the first 3 months can prevent development of corneal scarring and help surgical teams plan appropriate timing of eyelid and orbital reconstructive surgery.

Epidemiology

TCFS is present in 1 in 25,000–50,000 births. There is no gender, racial, or geographic predisposition to TCFS.

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Treatment for Lid Retraction

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Definition

Management of lid retraction based on the etiologic factors underlying the retraction.

Indication

In some cases, eyelid retraction may resolve spontaneously without any intervention. However, in most cases supportive treatment is indicated for exposure keratopathy secondary to eyelid retraction. This includes artificial tears, lubricants, ointments, and punctual plugs. In addition, retraction associated with systemic disease may improve with appropriate systemic therapy. For example, lid retraction related to Graves' disease may show improvement with corticosteroids or radiotherapy. In select cases, surgical management may be required to restore normal eyelid position or to correct severe exposure keratopathy. Surgery is usually indicated only after serial measurements have established stability of the disease for at least 6 months.

Contraindication

Surgical repair is contraindicated if preoperative serial lid measurements are fluctuating unless vision-threatening corneal decompensation is present.

Techniques and Principles

The approach to surgery is directed by etiologic factors or deficiency underlying the retraction. For upper eyelid retraction, excision of Müller's muscle with recession of levator aponeurosis may be performed. Spacers may be used to lengthen the upper eyelid and may include contralateral torus and autologous sclera. Fascia lata, ear cartilage, or alloplastic materials are also used.

For lower eyelid retraction, the surgical technique depends on whether anterior, middle, or posterior lamellar deficiency is present and severe cases require use of a spacer such as auricular cartilage or hard palate mucosa. Correction may also require repair of canthal tendon laxity with lateral canthal tightening or elevation.

Outcome

The goal of surgical repair of lid retraction is restoration of normal eyelid position and minimization of secondary corneal exposure.

Complications

The most common postoperative complications for eyelid retraction are undercorrection and overcorrection of lid position. Postoperative shrinkage of spacers such as sclera may result in recurrence of lid retraction. Spacers can also cause corneal irritation and abrasion.

Cross-References

- ▶ Graves' Disease
- ▶ Lower Lid Retraction
- ▶ Upper Lid Retraction

Further Reading

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Trichiasis

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Synonyms

Misdirected eyelashes

Definition

Trichiasis is misdirection of the eyelashes so that they turn inward toward the cornea and conjunctiva, with or without inward turning of the eyelid (entropion). The inward turning of the lashes toward the cornea and conjunctiva can lead to irritation and inflammation of these ocular structures.

Etiology

Causes of trichiasis can be broadly divided into the categories of inflammation/infection (chronic blepharitis, trachoma, herpetic disease), tumors (basal cell carcinoma, capillary hemangioma, conjunctival amyloidosis), medications (epinephrine, pilocarpine, trifluridine, vidarabine), systemic autoimmune disorders (ocular cicatricial pemphigoid, erythema multiforme, Steven-Johnson syndrome), and trauma (chemical injury, thermal burn, surgical trauma) (Cat and Burkat 2011).

Clinical Presentation

The patient may present with symptoms of eye irritation, foreign body sensation, or blurred vision. However, trichiasis itself may be a manifestation of numerous disease processes as mentioned in the etiology section, and a careful clinical exam and work-up may be needed to determine the cause.

Diagnosis

Trichiasis can be a manifestation of a serious disease process and recognition, and diagnosis of the underlying disease pathology is key in its management, and a biopsy should be performed whenever indicated.

Differential Diagnosis

The differentials of trichiasis include the different disease processes that can manifest as trichiasis as noted in the etiology section.

Prophylaxis

Trichiasis from recurrent trachoma infections can be prevented by treating trachoma with antibiotics and implementing hygienic measures (Prevention 2013).

Therapy

When trichiasis is associated with symptoms or is leading to damage to the ocular tissues, it should be treated. Electrolysis, cryotherapy, mechanical epilation, surgery, and argon laser lash ablation are some of the treatment modalities that have been employed in the treatment of trichiasis. The mode of treatment depends on various factors including disease etiology, pattern, and extent of involvement (i.e., segmental or diffuse and the number of lashes involved) and whether there is coexisting entropion present.

Mechanical epilation is convenient and associated with low cost. The extremely high recurrence rate makes it a suboptimal method for long-term control of the disease process. However, it is a good approach for a patient who comes in to the clinic with 1 or 2 lashes affected and no prior history of trichiasis (Kersten and McCulley 2011).

Electrolysis destroys the lash follicle with electrical current. It can lead to eyelid scarring, and the recurrence rate remains high.

Cryotherapy can lead to complications such as loss of all lashes, trichiasis in adjacent areas, loss of meibomian glands, loss of skin pigment, reactivation of herpes zoster, as well as eyelid complications such as eyelid edema and lid notching (Kersten and McCulley 2011).

Argon laser can also be used for ablation of aberrant eyelashes. Bartley et al described their experience in using argon laser for treatment of trichiasis in 44 patients with follow-up intervals ranging from 1 month to over 4 years. They reported that ablation of misdirected lashes was accomplished with one treatment in over half the patients. They noted that the laser treatment may be less effective than cryotherapy for treatment of trichiasis but it incited less post-procedural inflammation and maybe useful in cases such as ocular pemphigoid (Bartley and Lowry 1992).

Basar et al described their experience in using argon laser for treatment of 60 eyelids of 45 patients with trichiasis. They used topical anesthesia, 1 watt power for 0.20 seconds and 100 micron beam diameter which was directed coaxially to the lash follicle to create a 2-3mm crater, once a crater was observed the laser settings were changed to 1.2watt power for 0.2 seconds and 200 micron beam diameter. Patients were followed for an average of 6 months and 25% had recurrence. Side effects of treatment included mild hypopigmentation in three cases and mild lid notching in another three (Basar et al. 2000).

When trichiatic lashes involve the entire lower eyelid margin, there is usually associated cicatrization of the conjunctiva. Tarsotomy is an effective procedure in case of diffuse trichiasis. Tarsotomy can be performed with local anesthesia and involves rotating the eyelid margin using sutures passed from the conjunctival surface to the skin surface adjacent to the lashes. Another surgical technique that can be used is called the "4-snip" procedure. This involves a full thickness eyelid resection in the area of trichiasis in conjunction with lid margin rotation (Allen 1991).

Prognosis

If left untreated, trichiasis can lead to multiple ocular complications including corneal scarring leading to blindness (Thylefors et al. 1995).

Epidemiology

Trichiasis when associated with trachoma is the leading infectious cause of blindness worldwide. It is estimated that active trachoma affects 150 million people worldwide, and of these over 10 million have trichiasis, and about 6 million have blinding corneal scarring (Thylefors et al. 1995).

Cross-References

- ▶ Chlamydia
- ▶ Distichiasis: Definition
- ▶ Ocular Cicatricial Pemphigoid (OCP)

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Trichilemmal Cyst

▶ Epidermal Cysts, of the Eyelid
▶ Sebaceous Cyst

Trichilemmoma

▶ Lash Follicle, Tumors Arising in

Trichinella spiralis Trichinosis, Orbital Infection Caused by

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Definition

Trichinosis is an infection by any of the three species of roundworm: *Trichinella spiralis* (predominantly infects pigs), *Trichinella pseudospiralis* (parasite of raccoons, cats, mice, and birds), or *Trichinella britovi* (parasite of foxes) (Capo and Despommier 1996).

Etiology

All three species of *Trichinella* may infect humans; however, *T. spiralis* is the most common (Harms et al. 1993). Infection occurs by consuming raw or improperly cooked meat, containing the encysted larvae, particularly pork. The worms are 1.2–4 mm long and approximately 40–60 μm in diameter. Female worms are larger than male worms. After consumption of infected meat, the encysted larvae quickly mature over 36 h into an adult form. The adult *T. spiralis* mates in the small intestine of the host where the male worms die after copulation, and the female worms live in the small intestinal crypts to give birth to thousands of immature first-stage larvae which gain entrance to the systemic circulation through the portal system. These larvae then migrate to skeletal muscles including extraocular muscles where they encyst (Capo and Despommier 1996; Roos 2005).

Epidemiology

This parasite is endemic to areas of Africa, Mexico, Central and Northern South America, and Southeast Asia. Trichinosis is one of the more common helminthic zoonoses worldwide. There are eight *Trichinella species*; five species are encapsulated and three are nonencapsulated. Only three *Trichinella* species are known to cause trichinosis: *Trichinella spiralis* (predominantly infects pigs), *Trichinella pseudospiralis* (parasite of raccoons, cats, mice, and birds), or *Trichinella britovi* (parasite of foxes). Approximately 11 million individuals worldwide are infected with *Trichinella.* It is rare to find trichinosis today in developed countries. From 1997 to 2001, an annual average of 12 cases per year was reported in the United States (Roos 2005).

Clinical Presentation

Clinical features are divided into three phases (Capo and Despommier 1996; Roos 2005). The first phase (enteric phase) occurs after consumption and consists of gastrointestinal symptoms

generally within 48 h of ingestion. The second phase (invasive phase) occurs during larvae migration in systemic circulation and provokes a systemic allergic response with the "classic features" of high fever (~104 °F), myalgia, palpebral eyelid and facial edema, and eosinophilia over the course of 2–8 weeks. This high fever is atypical of other helminthic infections. The larvae may disseminate into multiple organs such as the brain, heart, lung, and kidneys. Larvae migration to the eye frequently invades the extraocular muscles (Roos 2005). When extraocular muscles are involved, ophthalmoplegia, proptosis, and pain with eye movements develop. Other ocular findings such as subconjunctival hemorrhage, conjunctival chemosis, retinal hemorrhages, chorioretinitis, and optic neuritis may occur. CNS infection, if present, usually requires large numbers of organisms with accompanying myocarditis. The clinical manifestations of trichinosis are found in the following frequency: muscular (90%), ocular (59%), neurological (52%), and psychological (52%). The third phase coincides with cyst formation (encystment phase).

Diagnostics

Since it is rare to recover this organism in the feces, diagnosis is made based on clinical history and by biopsy of striated muscle (often from the calves) or intestinal tract or serologically by ELISA. Eosinophilia and country of origin are important clinical information to have a high index of suspicion of this disease entity since eosinophilia is usually the earliest indicator of infection. Elevated creatinine phosphokinase may also be seen due to myositis (Capo and Despommier 1996).

Differential Diagnosis

- ▶ Contact Dermatoblepharitis
- ▶ Diplopia in Multiple Sclerosis
- ▶ Intraocular Lymphoma
- ▶ Pseudotumor Cerebri

Prophylaxis

None. Always eat well-cooked meats by cooking to an internal temperature of 165 °F (74 °C) for a minimum of 15 s. Freezing pork less than 6 in. thick for 20 days at 5 °F will also kill any worms.

Treatment

Treatment is targeted at encysted larvae and adult forms with anthelmintics: mebendazole (200–400 mg three times a day for three days) or albendazole (400 mg twice a day for 8–14 days) are given to treat trichinosis (Roos 2005). Common side effects of these medications are nausea, vomiting, diarrhea, and abdominal pain. High drug dosages may cause liver enzyme elevations, agranulocytosis, and alopecia. However, no specific treatment exists against encysted larvae. Caution should be taken when treating trichinosis due to a severe inflammatory response secondary to antigens released, in particular if larvae are present in the brain. Prednisone has been utilized to decrease tissue damage; however, its use is controversial. Common dosage of prednisone ranges from 20 to 60 mg per day. NSAIDs may be used to help control symptoms. The primary mainstay of treatment is aimed at prevention.

Prognosis

The vast majority of patients (90–95%) who acquire trichinosis have minor symptoms. These patients do well and do not develop complications. Patients who acquire more serious systemic infections have unclear prognosis, especially with CNS involvement since the encysted larva may persist for many years.

References

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Trichoadenoma

► Lash Follicle, Tumors Arising in

Trichoepithelioma

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Synonyms

Solitary trichoepithelioma

Multiple adenoid cystic epithelioma or Brooke's tumor.

Definition

A benign adnexal tumor of hair follicle origin and most commonly found on the face and eyelids.

Etiology

Sporadic when solitary or possibly genetic, especially in the inherited (autosomal-dominant) form with multiple lesions (Albert and Jakobiec 2008; Shields and Shields 2008).

Clinical Presentation

Solitary or with multiple lesions. Typically occurring in young to aging adults; however, the hereditary form may be seen in younger individuals.

Solitary trichoepithelioma appear as an asymptomatic, flesh-colored, firm nodular, lesions, usually on the face. Telangiectatic vessels may be seen. This nonhereditary tumor may be difficult to distinguish from a basal cell carcinoma; ulceration may occur rarely. Multiple trichoepitheliomas generally begin during early childhood or at puberty as firm skin-colored papules and nodules (2–8 mm) on the nasolabial folds, facial skin, and eyelid. They may gradually increase in size and number (Albert and Jakobiec 2008; Shields and Shields 2008).

Diagnostics

Based on history, clinical examination, and confirmed by histopathological examination after biopsy.

Differential Diagnosis

Differential diagnosis includes ► basal cell carcinoma, ► angiofibroma, ► syringoma, and ► trichofolliculoma

Prophylaxis

Unknown.

Therapy

Surgical excision. Carbon dioxide laser may be an alternative.

Prognosis

Slow growth is characteristic. Although rare, malignant transformation may occur. In cases of multiple facial lesions, cosmetic disfigurement may be of concern (Albert and Jakobiec 2008; Shields and Shields 2008).

Epidemiology

Unknown.

Cross-References

► Angiofibromas, Facial, in Tuberous Sclerosis
► Basal Cell Carcinoma of Eyelid
► Lash Follicle, Tumors Arising in
► Trichofolliculoma

References

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Trichofolliculoma

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Synonyms

Hamartoma of hair follicle

Definition

Trichofolliculoma is a benign neoplasm of hair follicles.

Etiology

The precise etiology is uncertain but seems to develop spontaneously and with no association with systemic disease or other skin disorders (Albert and Jakobiec 2008; Shields and Shields 2008).

Clinical Presentation

Solitary, slow growing tumors, most commonly found on the face, scalp, neck, or on the eyelid margin. The lesion is a firm, small, slightly elevated, skin-colored nodule with a central pore or depression containing keratinous material or a wisp of wool-like or cottony hairs, usually white and short, protruding from or growing out of it (Albert and Jakobiec 2008; Shields and Shields 2008).

Diagnostics

By characteristic appearance of central umbilication and protruding hair. Confirmed by histopathological examination.

Differential Diagnosis

Differential diagnosis includes ▶ basal cell carcinoma, ▶ molluscum contagiosum, ▶ syringoma, ▶ trichoepithelioma, ▶ sebaceous cyst, and ▶ nevus.

Prophylaxis

Unknown.

Therapy

Surgical excision.

Prognosis

Excellent. If incompletely excised, recurrence may occur.

Epidemiology

Rare.

Cross-References

- ▶ Basal Cell Carcinoma of Eyelid
- ▶ Blue Nevus
- ▶ Lash Follicle, Tumors Arising in
- ▶ Molluscum Contagiosum
- ▶ Trichoepithelioma

References

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Tricinolon

► Intravitreal Triamcinolone

Trigeminal Ganglion

► Gasserian Ganglion (Semilunar/Trigeminal Ganglion)
► Trigeminal Ganglion (Gasserian/Semilunar Ganglion)

Trigeminal Ganglion (Gasserian/Semilunar Ganglion)

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Synonyms

Gasserian ganglion; Semilunar ganglion; Trigeminal ganglion

Definition

Afferent sensory fibers of the trigeminal nerve originate from cell bodies within the *trigeminal ganglion*. A fold of dura, named Meckel's cave, houses the sensory trigeminal ganglion also known as the Gasserian or semilunar ganglion. Two of the three branches (V1 and V2) of the trigeminal nerve serve solely as sensory nerves, whereas the mandibular division (V3) of the trigeminal nerve has both motor and sensory fibers.

The sensory root of CN V exits the pons ventrally and fans out to form the trigeminal ganglion; meanwhile, the motor fibers of CN V remain separated. Three separate sensory divisions then come off the trigeminal ganglion and continue as the ophthalmic nerve (V1), maxillary nerve (V2), and mandibular nerve (V3).

Cross-References

► V1 (Ophthalmic Nerve)
► V2 (Maxillary Nerve)
► V3 (Mandibular Nerve)

Further Reading

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Trigeminal Nerve

► Cranial Nerve V (Trigeminal Nerve)

Trimalar Fracture

► Zygomatic-Maxillary Complex Fractures

Tripod Fracture

► Zygomatic-Maxillary Complex Fractures

Trochlear Nerve

► Cranial Nerve IV (Trochlear Nerve), CNIV

Trochlear Nerve Palsy

► Fourth Nerve Palsy

Trypan Blue

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Definition

Dye derived from toluidine.

Indication

Staining of the anterior capsule in cataract surgery, in pediatric cataract surgery, and in cataract surgery lacking a good red fundus reflex (e.g., white cataracts, corneal opacities) and staining of epiretinal membranes in vitreoretinal surgery.

Contraindication

Trypan blue should only be used in pregnant women when the potential benefit justifies the potential risk to the fetus.

Use and Dosage

For capsulorhexis, trypan blue ophthalmic solution is usually applied in a concentration of 0.06%. However, concentrations up to 1% have been applied (Farah et al. 2009). The dye is injected directly on top of the anterior lens capsule under an air bubble. The air bubble limits contact of the dye to the iris and the anterior capsule. Alternatively, trypan blue may be mixed with viscoelastic or instilled under viscoelastic. After approximately 5 s of staining, the anterior chamber is irrigated using balanced saline solution prior to performing capsulorhexis. In chromovitrectomy, trypan blue is applied to stain epiretinal membranes, and it also stains the internal limiting membrane to some degree. Trypan blue (0.06–0.15%) is injected into the posterior pole after fluid–air exchange and is washed out with balanced salt solution (Heilweil et al. 2010).

Adverse Reactions

Trypan blue is labeled by the FDA as a mutagen in the Ames test and as a carcinogen in rats. However, there are data that confirm that the dye is safe and effective as an adjunct for capsule visualization in cataract surgery (Jacobs et al. 2006). There are anecdotal reports that permanent discoloration of a hydrophilic acrylic intraocular lens requiring explantation of the lens has occurred (Saini et al. 2003). Clinical studies and morphologic analysis of trypan blue-assisted vitreoretinal surgery revealed no toxic effect to the human retina. However, there is controversy in experimental data suggesting a dose-dependent retinal damage after trypan blue exposure (Werner et al. 2002).

Cross-References

► Cataract Surgery
► Posterior Capsulorhexis

References

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Tumors of Apocrine Origin

► Sweat Glands of Eyelid, Tumors Arising in

Tumors of Eccrine Origin

► Sweat Glands of Eyelid, Tumors Arising in

Tumors of Pilar Origin

► Lash Follicle, Tumors Arising in

Tunneling

► Clear Corneal Incision

Turner-Kieser Syndrome

► Onychoosteodysplasia (Nail-Patella Syndrome)

TVOs

► Transient Obscurations of Vision

Two-Snip Procedure

► Wies Repair

Type-II Vascular Malformation

► Varices, Orbital

U

UBM

► Biomicroscopy, Ultrasound
► Biomicroscopy, Ultrasound, of Anterior Segment

Ulcerative Keratitis

► Ulcers

Ulcerative Keratitis Disease

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Synonyms

Bacterial keratitis with ulceration; Corneal ulceration; Fungal keratitis with ulceration; Infectious keratitis with ulceration; Noninfectious keratitis with ulceration; Viral keratitis with ulceration

Definition

Ulcerative keratitis refers to the disruption of the corneal surface and/or deeper layers, often associated with inflammation.

Etiology

Ulcerative keratitis may be sterile or infectious. Infectious keratitis may be caused by bacterial, viral, fungal, or parasitic organisms. Important historical clues for an infectious etiology include contact lens use, trauma, foreign body, previous ocular surgery, and exposure to contaminated water (Karp and Forster 2011). Bacterial keratitis usually only develops after ocular immune defenses have been compromised. However, there are some bacteria that are able to penetrate a normal corneal epithelium. These bacteria include *Neisseria gonorrhoeae*, *N. meningitidis*, *Corynebacterium diphtheriae*, and *Haemophilus influenzae.* The most common pathogens are *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Streptococcus* (Kanski and Bowling 2011).

Contact lens use and abuse has been a major contributor to the development of ulcerative keratitis. Extended wear contact lenses have been associated with an increased risk of keratitis. Outdoor trauma involving soil or vegetation may be suggestive of an infection involving fungi or another fastidious organism (Karp and Forster 2011). Diseases, such as herpes simplex keratitis and keratoconjunctivitis sicca, may be complicated by ulcerative keratitis (Ferri 2009). Up to 60% of corneal ulcers in developing countries may be complications of herpes simplex virus infections (Kanski and Bowling 2011).

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Stromal keratitis may result from impaired local host defenses. Chemical injury, neurotrophic disease, tear insufficiency, stem cell deficiency, bullous keratopathy, previous herpetic disease, topical anesthetic use, and topical corticosteroid use are important historical factors that suggest impaired local defenses (Karp and Forster 2011). Systemic diseases, such as acquired immunodeficiency syndrome (AIDS), diabetes mellitus, malnutrition, and alcoholism, may contribute to increased risk of keratitis. Immunosuppressive treatments for systemic inflammatory diseases, such as rheumatoid arthritis, Wegener's granulomatosis, and Sjogren's syndrome, may also predispose patients to keratitis development (Karp and Forster 2011). Ulcerative keratitis may be associated with collagen vascular disease or exophthalmos secondary to thyroid disease (Ferri 2014).

Mooren's ulcer is a rare, idiopathic condition that causes peripheral stromal ulceration that progresses centrally. There are two types of Mooren's ulcers. One type affects older individuals predominantly and tends to be unilateral. This type tends to respond well to medication. The second type is more aggressive, affects younger individuals, tends to be bilateral with severe pain, and is less responsive to treatment. The second type is thought to have an autoimmune mechanism, and there is often a history of corneal insult that is thought to act as a trigger in susceptible individuals (Kanski and Bowling).

Clinical Presentation

Ulcerative keratitis is characterized by sloughing of the corneal epithelium and keratolysis, also known as corneal melting (Soukiasian 2014). It presents as a localized, well-demarcated lesion with a corresponding focal ulcer or yellow-white stromal suppuration with thick mucopurulent exudate and edema. The eye is typically red with infiltration in the surrounding cornea. The corneal ulcer may be painful with associated conjunctival edema and infection (Ferri 2009). Affected individuals may experience foreign body sensation, pain, and photophobia when the corneal epithelium erodes and ulcerates. Vision may be impaired if the inflammation involves the central cornea or from induced astigmatism. Anterior uveitis may be associated with ulcerative keratitis, and it contributes to photophobia and visual impairment. The characteristic features include epithelial loss, various degrees of stromal infiltration, and thinning secondary to keratolysis. Mooren's ulcer tends to be chronic and extremely painful. It begins in the periphery, adjacent to the sclera with a steep, undermined, or overhanging central margin with an occasionally infiltrated leading central border. It is not typically associated with scleritis (Soukiasian 2014).

S. aureus infections typically progress slowly (Karp and Forster 2011). Staphylococcal marginal ulcers begin as an infiltrate adjacent to the limbus with a clear zone between, which progresses and leads to ulceration (Soukiasian 2014). Streptococci tend to cause an acute and highly suppurative reaction with deep central stromal ulceration and an advancing edge of infection. Infectious crystalline keratopathy (ICK) is a unique presentation of streptococcal infection that occurs at the graft-host junction following keratoplasty (Karp and Forster 2011). Viral keratitis is often highly contagious (Ferri 2014).

Sterile neurotrophic ulcers are typically associated with tissue breakdown but no pain (Ferri 2009). Stromal ulceration secondary to immune-related pathology may present with varying degrees of cellular infiltration. Such ulceration may be associated with scleritis, episcleritis, or iritis (Karp and Forster 2011). Corneal melting occurs in response to enzymatic activity in peripheral ulcerative keratitis (Kanski and Bowling 2011). Once corneal melting begins, the process may progress rapidly. Ulcerative keratitis may progress to perforation if left untreated. It may be life threatening when associated with a systemic autoimmune condition (Soukiasian 2014).

Diagnosis

A thorough history should be obtained, including history of ocular infections, contact lens wear, current and previous medications, trauma, and

previous eye surgery or laser vision correction procedures (Soukiasian 2014). Microscopic examination of both eyes should be done with a slit lamp and fluorescein staining (Ferri 2014). The lids, lashes, and conjunctiva should be evaluated for inflammation secondary to rosacea, seborrhea, and mechanical lid dysfunctions. The lacrimal system should be assessed for adequate tear function and underlying dacryocystitis or canaliculitis that may compromise corneal health. Careful evaluation of the corneal stroma of the fellow eye should be performed to rule out a peripheral immune-mediated marginal keratitis (Karp and Forster 2011). Culture of ulcer scrapings should be done for definitive etiologic diagnosis (Ferri 2009).

Differential Diagnosis

The differential diagnosis for ulcerative keratitis includes various infections. More virulent pathogens include *Pseudomonas* and pneumococcus. *Moraxella*, *Staphylococcus*, and alpha-hemolytic *Streptococcus* are less virulent pathogens that may be involved. Viruses, such as herpes simplex, may cause infection leading to ulceration. Contact lens ulcers should also be considered (Ferri 2009). Peripheral immune-mediated marginal keratitis may be seen in rheumatoid arthritis, Wegener's granulomatosis, and Mooren's ulcer. These are rarely infectious (Karp and Forster 2011). Patients with autoimmune disease-associated ulcerative keratitis may become secondarily infected, and thus infectious causes must be ruled out by the initial work-up. Ulceration without inflammation and typically an intact corneal epithelium is suggestive of a noninflammatory etiology, such as Terrien's marginal degeneration, pellucid marginal degeneration, and marginal furrow (Soukiasian 2014).

Prophylaxis

Prophylactic topical antibiotics are sometimes used to prevent secondary infections in cases of peripheral ulcerative keratitis (Soukiasian 2014).

Therapy

Ulcerative keratitis therapy includes warm compresses and patching of the affected eye. Contact lens wear should be discontinued. Intense antibiotic and antiviral therapy should be initiated (Ferri 2009). Bacterial infections may be treated with subconjunctival cefazolin or gentamicin (Ferri 2014). NSAIDs may be used. In cases of fungal infections, patients should be hospitalized, and topical antifungal agents should be initiated (Ferri 2009). Topical anesthetics or steroids should never be used in cases of ulcerative keratitis. Anesthetics and steroids may aggravate fungal or herpetic ulcers, leading to perforation of the cornea (Ferri 2014).

Systemic corticosteroids such as oral prednisone are commonly used in the acute management of severe peripheral ulcerative keratitis secondary to autoimmune etiologies. If the ulceration progresses, pulsed administration of methylprednisolone may be effective. The prolonged use of systemic corticosteroids may result in significant systemic side effects. In cases of potential perforation, systemic corticosteroids may be combined with immunosuppressive therapy. Systemic immunomodulatory therapy becomes necessary when local therapy fails; there is an associated collagen vascular disease or bilateral Mooren's disease. The presence of a vasculitis, particularly suggested by a concurrent associated scleritis, is a key factor in deciding to initiate treatment with immunosuppressive agents as it suggests systemic collagen vascular disease. Peripheral ulcerative keratitis secondary to Wegener's granulomatosis is treated with an immunosuppressive, such as cyclophosphamide, with corticosteroids. Methotrexate would be useful in maintenance therapy. The efficacy of biological agents, such as anti-tissue necrosis factor (TNF) and anti-B cell monoclonal antibodies, has not been established for treatment of peripheral ulcerative keratitis, but the established efficacy of these drugs in treatment of systemic inflammatory diseases is promising (Soukiasian 2014).

Surgical treatments may be used palliatively in peripheral ulcerative keratitis to maintain the integrity of the globe. Surgery is not effective as

a monotherapy as it does not affect the underlying immunologic process. Conjunctival resection may temporarily remove the local cellular mediators and collagenases that cause progression of the disease process. Cyanoacrylate adhesive combined with immunosuppressive therapy may help to delay impending perforation and the need for tectonic corneal surgery (Soukiasian 2014).

Prognosis

Ulcerative keratitis secondary to an immune-related process may maintain good visual function if the inflammatory process is controlled without delay. The prognosis is more guarded if the ulceration is associated with systemic collagen vascular disease. Peripheral ulcerative keratitis with associated scleritis typically has a worse prognosis than scleritis alone. Significant visual impairment and ocular morbidity may result in cases of corneal perforation. Cataracts or glaucoma may result from the inflammatory process of peripheral ulcerative keratitis or the use of corticosteroids (Soukiasian 2014).

Epidemiology

Ulcerative keratitis affects men and women equally, and it can affect individuals of all ages. The average general ophthalmologist observes four to six cases of ulcerative keratitis each month (Ferri 2014). Almost 50% of individuals with peripheral ulcerative keratitis have an associated systemic disease, most commonly a collagen vascular disease. Up to 25% of peripheral ulcerative keratitis patients experience ulcerative keratitis as a presenting feature of a potentially undiagnosed systemic vasculitis. Rheumatoid arthritis is the most common collagen vascular disease associated with peripheral ulcerative keratitis (Soukiasian 2014).

Cross-References

- ▶ Corticosteroids, Use in Ophthalmology
- ▶ Herpes Simplex Virus
- ▶ Herpes Zoster Ophthalmicus
- ▶ Keratitis

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Ulcerative Keratopathy, Toxic

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Synonyms

Toxic ulcerative keratopathy

Definition

The most severe manifestation of toxic keratoconjunctivitis (keratoconjunctivitis medicamentosa) (Albert et al. 2008).

Etiology

Toxic ulcerative keratopathy is a result of overtreatment by topical ophthalmic medication (Schwab and Abbott 1989). Preservatives in eye drops such as benzalkonium chloride and thimerosal are the most common cause of toxicity. Preservatives serve as antimicrobials in solution but can lead to epithelial toxicity and irreversible corneal edema (Holland et al. 2013).

Over-the-counter eye drops, glaucoma medications (e.g., pilocarpine, carbachol), antivirals (e.g., trifluorothymidine), antibiotics (e.g., gentamicin), and anesthetics (e.g., proparacaine) are all examples of medications that may cause toxic ulcerative keratopathy by interfering with epithelial cell membrane physiology.

Toxicity can be caused by the medication itself, from preservatives in solution or from its degradation products (Schwab and Abbott 1989; Krachmer et al. 2010). Solutions can be toxic to the ocular surface due to photosensitization of the eye, osmolarity of the solution, or sensitivity to the pH of the solution. Ophthalmic treatments may be directly toxic by initiating a cascade of events in the eye that manifest after a threshold of toxicity is reached. Toxicity can also be indirect by manifesting as a result of a condition caused by the ophthalmic medication. For example, decreased tear production and cytotoxicity to goblet cells can lead to epithelial effects. Antimicrobial preservatives in solution can sometimes create an environment favorable to the growth of bacteria. Toxicity can be caused by a combination of various mechanisms or can be the result of a single mechanism. It can develop either immediately or after many years of use of ophthalmic medication (Holland et al. 2013). Toxicity may be self-induced (factitious) by the abuse of over-the-counter or prescription eye drops or iatrogenic (Albert et al. 2008).

Clinical Presentation

Toxic keratoconjunctivitis can be a precursor to the development of toxic ulcerative keratopathy. The effects of keratoconjunctivitis are localized to the inferonasal quadrant but are still more diffuse than the effects of toxic ulcerative keratopathy. The disease usually manifests as coarse and punctuate epithelial lesions with heaps and swirls of opaque epithelium. Pseudodendrites resembling herpetic dendrites may also develop (Krachmer et al. 2010).

Toxic ulcerative keratopathy is the most severe manifestation of toxic keratoconjunctivitis. Patients present with a characteristic oval epithelial defect located mainly in the inferonasal quadrant, where there is usually maximal contact between the drug and the surface of the eye (Krachmer et al. 2010; Holland et al. 2013). These defects can be round to oval without being ragged or irregular. The edges of the defect are gray and rolled up without prominent margins. The disease can be characterized by a "comet's impact crater," with the epithelial defect as the crater, surrounded by a severe, coarse superficial keratitis (Schwab and Abbott 1989). The most severe keratopathy is closest to the crater. Stromal edema is usually present, and epithelial edema may be a characteristic as well. Mucous threads, intense ciliary flush, papillary tarsal response, and chemosis may also be present (Krachmer et al. 2010).

Diagnostics

Recognition of toxicity is essential to treatment. Toxicity should be considered in the case of a chronic ocular irritation that does not improve with treatment. When toxicity is not recognized, increased doses of medication can exacerbate the underlying toxic ulcerative keratopathy. The patient interview is fundamental to gaining awareness of factitious cases of toxicity (Krachmer et al. 2010). Patients often neglect mentioning the use of over-the-counter eye drops, particularly in cases of abuse (Holland et al. 2013). Examination of clinical symptoms is also essential in diagnosis. Epithelial defects in the conjunctiva and cornea stain well with fluorescein and rose bengal dyes (Schwab and Abbott 1989; Albert et al. 2008).

Lab tests such as conjunctival biopsy, conjunctival scraping, and impression cytology, though not commonly performed, can also be used to assess toxicity. Conjunctival biopsies are not well tolerated by patients and test for autoimmunity and toxicity. A common finding of such biopsies regarding toxic damage shows squamous metaplasia of the conjunctival epithelium, subconjunctival inflammation, and fibrosis, particularly in patients who used glaucoma medications. Conjunctival scraping is typically only used to test

for allergy and infection but can also test for toxicity. Impression cytology provides a homogenous cell layer for studies that determine the cell types, cytokines, and membrane, and cytoplasmic inflammatory markers present in the conjunctival epithelium (Holland et al. 2013).

Differential Diagnosis

Differential diagnoses include punctate keratopathy and neurotrophic keratitis, which presents with an ulcer with rolled edges, similar to ulceration in toxic ulcerative keratopathy (Holland et al. 2013). Patients with iatrogenic toxic ulcerative keratopathy often present with other ocular diseases such as herpes simplex infection, herpes zoster infection, previous ocular surgery, and ▶ keratoconjunctivitis sicca. Toxic ulcerative keratopathy may be misconstrued as worsening of the disease for which the drops were administered (Schwab and Abbott 1989).

Prophylaxis

Unclear

Therapy

Treatment involves terminating the use of the offending medication and replacement with oral medication or preservative-free topical solution. Non-preserved ointments may provide symptomatic relief. Patching with the use of viscoelastic agents or therapeutic soft contact lenses are also useful in the treatment of epithelial defects (Schwab and Abbott 1989). In severe cases, conjunctival flap procedures or keratoplasty may be needed (Krachmer et al. 2010). In factitious cases, counseling, therapy, or psychiatric help may be warranted (Schwab and Abbott 1989).

Prognosis

Most patients heal, with only a slight vortex fluorescein-staining pattern on the epithelium (Schwab and Abbott 1989).

Epidemiology

Toxic keratoconjunctivitis is one of the most-frequent problems seen by corneal specialists. Toxic ulcerative keratopathy is a more rare manifestation of toxic keratoconjunctivitis (Albert et al. 2008).

Cross-References

▶ Keratoconjunctivitis: Overview

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Ulcers

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Synonyms

Ulcerative keratitis

Definition

A loss of corneal tissue with associated inflammation.

Etiology

A corneal ulcer rarely occurs in healthy tissue and is usually associated with alteration in one of the

following: structure, immunity, innervation, or defense mechanism. The key question in initial diagnosis is if the ulcer is infectious or sterile. Risk factors include contact lens use, previous surface disease, trauma, and previous surgery (Green et al. 2008).

Infectious causes include bacterial, viral, fungal, and protozoan. The most common species of each group varies on geographic location. However, generally gram-positive cocci and gram-negative rods are common.

In the United States, the most common bacterial organisms are *Staphylococci* and *Pseudomonas*. Fungal causes include *Fusarium* and *Aspergillus*. Herpes simplex virus (HSV) and varicella zoster virus (VZV) are common viral causes. *Acanthamoeba*, a protozoa, is a relatively rare cause of corneal infection but deserves mention due to the difficulty in management and severe vision loss that results (Mascarenhas et al. 2014).

Sterile causes are due to systemic inflammatory conditions and neurotrophic cornea. If a sterile cause is suspected, it is important to obtain a complete medical history including a history of rheumatoid arthritis (RA), Wegener's granulomatosis, and Sjögren's syndrome. A neurotrophic cornea is usually due to a fifth nerve palsy or from recurrent infections usually with HSV or VZV. It results in impaired epithelial healing leading to inflammation and at times a secondary microbial infection.

Clinical Presentation

Presentation is variable depending on many factors including infectious organism, length of infection, immune status, corneal status, and history of antibiotic and steroid use. Corneal ulcers often present with red eye, decreased vision, ocular pain, tearing, and photophobia. These symptoms are usually rapid in onset. By diagnosis, all corneal ulcers have an epithelial defect and an inflammatory infiltrate which would be evident on slit-lamp exam.

Infectious ulcers generally are associated with corneal infiltration and are more purulent. There is also a higher chance of an anterior chamber reaction (AC) causing a hypopyon and corneal endothelial plaques.

Fungal ulcers often have satellite lesions and are more feathery in appearance. *Acanthamoeba* ulcers usually have pain out of proportion to exam, pseudodendrites early in presentation, and a ring infiltrate in later presentation (Mascarenhas et al. 2014).

Inflammatory ulcers also have an infiltrate associated but without a purulent reaction. There is also a less of an AC reaction.

Diagnostics (Lab Diagnostics)

The presence of epithelial defect and corneal infiltrate on slit-lamp exam. Initial exam should be detailed with measurements of both the infiltrate and epithelial defect. Measurements are followed closely to monitor for resolution.

Corneal scrapings for cultures and staining should be obtained especially for ulcers that have a chronic appearance, if the infiltrate is large, central, or deep. Polymerase chain reaction can also be done for viral diagnosis and if there is an atypical appearance with concern for fungal, protozoan, or mycobacterial causes (Krachmer and Mannis 2011).

For culture, topical anesthetic can be used. It is advised to use proparacaine hydrochoride 0.5% as other anesthetics can inhibit organism recovery. There are several instruments to choose from to obtain corneal scrapings including Dacron/calcium alginate or sterile cotton swab, a sterilized platinum spatula, or No. 15 Bard-Parker blade or jeweler's forceps. To obtain a maximum yield, several areas from the borders of the ulcers should be sampled. It is not sufficient to obtain only purulent material. If possible and/or clinically indicated, a culture of the patient's contact lenses, case, and solution may also be helpful in diagnosis of the causative organism (Krachmer and Mannis 2011).

Differential Diagnosis

Infectious versus noninfectious causes, corneal abrasion, corneal trauma, chemical injury, and foreign body.

Prophylaxis

Proper care for contact lenses.

Therapy

Wide-spectrum antibiotic drops are the mainstay in the initial treatment for infectious ulcers. Antibiotic ointments can be useful for less severe ulcers or as adjunctive therapy. The treatment should be tailored based on the response to antibiotics and also to results from cultures and sensitivities.

HSV and VZV are treated systemically with oral antiviral medications and occasionally with topical antivirals and topical steroids.

Fungal ulcers are treated with both oral and topical antifungal medications most commonly amphotericin B and natamycin.

Acanthamoeba is typically treated with the biguanides and chlorhexidine.

Sterile ulcers resulting from inflammatory conditions are treated with steroids. For resolution, the systemic condition must be treated and under control.

Mydriatic agents can also be used to dilate the patient to help with discomfort from photophobia.

Prognosis

Prognosis is dependent on many factors including causative organism, time to treatment, and compliance with treatment. Typically, prognosis is good, but this condition can be vision threatening due to perforation and opacification (Sirikul et al. 2008).

Epidemiology

Epidemiology varies depending on geographic location, type of ulcer, patient population, and climate (Sirikul et al. 2008). There are 30,000 cases of bacterial keratitis annually in the United States. Around 10–30 people in 100,000 contact lens wearers develop bacterial keratitis yearly in the United States (Krachmer and Mannis 2011).

Cross-References

- ▶ Bacterial Keratitis
- ▶ Corneal Abrasion
- ▶ Fungal Keratitis with Ulceration
- ▶ Infectious Keratitis with Ulceration
- ▶ Viral Keratitis with Ulceration

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Ullrich-Feichtiger Syndrome

- ▶ Cryptophthalmos-Syndactyly (Fraser) Syndrome

Ultrafast Laser

- ▶ Femtosecond Laser

Ultrashort Pulse Laser

- ▶ Femtosecond Laser

Ultrasonic Pachymetry

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Synonyms

Ultrasound pachymetry

Definition

Measurement of corneal thickness with ultrasound.

Purpose

Assessment of corneal thickness prior to refractive surgery or cross-linking. Corneal thickness plays also a role in the interpretation of the measured intraocular pressure in glaucoma assessed with applanation tonometry.

Principle

Ultrasonic pachymetry is based upon the differential return of the ultrasonic waves by varying tissue types in the eye. Sound waves are emitted by a piezoelectric crystal and delivered with a probe. For axial measurements, the probe is placed perpendicular to the corneoscleral surface. Ultrasonic pachymetry can either be performed with the contact method when direct contact between the corneal surface and probe is made or with immersion biometry applying an eyecup between the eyelids filled with immersion fluid (e.g., balanced salt solution, methylcellulose).

Indication

Keratorefractive surgery, glaucoma.

Advantage/Disadvantage

Ultrasonic pachymetry is a reliable method for measurement of corneal thickness. A correct position of the probe is mandatory during measurement, and the results depend on the experience of the examiner. In contrast to optical biometry, ultrasound biometry can be performed even with an opaque cornea. Compared with optical pachymetry, ultrasound pachymetry is more time-consuming and requires topical anesthesia of the eye. Optical pachymetry produces thickness maps which may be more useful in identifying early thickness changes, such as in forme fruste keratoconus. However, corneal thickness measurements differ between optical and ultrasound pachymetry. This has to be taken into account when results are interpreted.

Cross-References

▶ Biometry, Use and Principle of
▶ Pachymetry (Pachometry)

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Ultrasonography, in Orbital Evaluation

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Synonyms

Ultrasound

Definition

Orbital ultrasonography is a diagnostic imaging technique that uses the application of sound to evaluate orbital pathology.

Purpose

Orbital ultrasonography is a useful imaging modality in the evaluation of patients with orbital disorders.

Principle

Ultrasonography uses sound waves generated at frequencies greater than 20,000 Hz. The sound waves are reflected back to the transducer by tissue in its path, and a piezoelectric crystal in the transducer vibrates when it returns. This results in electrical impulses that are translated into data. Orbital tissue can be evaluated based on the principles of sound waves. Higher frequency waves penetrate less tissue but allow for better resolution, while lower frequency waves penetrate more tissue at the cost of resolution. Sound waves have higher velocity when traveling through solids than liquids. When they travel between tissue interfaces with different acoustic impedance, they can scatter, reflect, or refract. The sound waves that return to the transducer, or echoes, can be distinguished as hyperechoic, hypoechoic, or anechoic.

There are two main types of ultrasound used in ophthalmology. An A-scan, or time-amplitude scan, generates sound waves at 8 MHz and converts them into spikes that correspond with tissue interface zones. A B-scan, or brightness amplitude scan, generates sound waves at 10 MHz and produces a corresponding image. A B-scan allows for the assessment of the position and shape of a lesion. It also provides a description of its borders, the internal architecture of the structure, its reflectivity, and sound attenuation characteristics. In combination, they can accurately locate and diagnose many orbital pathologies.

Indication

Orbital tumors
Localization of foreign bodies
Thyroid eye disease
Orbital infection
Proptosis or globe malposition

Contraindication

Ruptured globe is a relative contraindication.

Advantage/Disadvantage

The advantage of ultrasonography in orbital evaluation is that it is minimally invasive with no exposure to radiation or contrast dyes, widely accessible, and relatively inexpensive. It does not require sedation or anesthesia for successful examination of an infant. It also provides real-time information to the clinician including compressibility, mobility, and vascularity of a lesion.

Disadvantages include significant interoperator variability and limited value in assessing lesions in the posterior orbit because of sound attenuation.

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Ultrasound

► Ultrasonography, in Orbital Evaluation

Ultrasound Pachymetry

► Ultrasonic Pachymetry

Upgaze Palsy

▶ Vertical Gaze Palsy

Upper Lid Loading

▶ Eyelid Weights
▶ Eyelid Weights, for Exposure Keratopathy

Upper Lid Retraction

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Definition

Eyelid retraction is the displacement of the normal position of the upper eyelid margin with respect to the limbus.

Basic Characteristics

Clinical Features

In most normal individuals, the upper eyelid margin rests 1–2 mm below the superior limbus. In upper eyelid retraction, the lid margin is elevated superiorly above this level, usually at or above the limbus, often with visible sclera. Lid retraction can lead to lagophthalmos and corneal exposure, leading to secondary epiphora and dry eye symptoms.

Examination

A complete ocular examination is indicated including measurements of the position of the upper eyelid with relation to the limbus. Other important measurements include the height of the palpebral fissure, degree of lagophthalmos, associated proptosis, levator muscle function, and distance from upper eyelid margin to the central corneal reflex. Radiological imaging such as computed tomography or magnetic resonance imaging may be helpful in the diagnosis of thyroid disease and orbital tumors.

Etiology

Eyelid retraction has many diverse causes including local, systemic, or central nervous system etiologies. In 1996, Bartley published a comprehensive classification scheme with three general mechanisms of lid retraction: myogenic, neurogenic, and mechanistic causes.

The myogenic causes of eyelid retraction include Graves' disease, which is the most common cause of both upper and lower eyelid retraction. Although the exact mechanism of retraction associated with Graves' disease is debated, histopathologic changes include inflammation, adipogenesis, and fibrous contraction of eyelid retractors. In addition, sympathetically innervated eyelid retractor muscles are preferentially affected. A common associated finding is lateral flare, in which the eyelid retraction is greater laterally than medially, resulting in an abnormal upper eyelid contour that appears to flare.

Other causes of myogenic eyelid retraction include botulinum toxin injection, congenital eyelid retraction, and postsurgical complications. The latter includes a change in eyelid position after vertical rectus muscle surgery, with anatomical connections between the superior rectus and levator muscles.

Neurogenic eyelid retraction is usually acquired but may be present at birth. More common causes include dorsal midbrain syndrome, aberrant regeneration or innervation of the oculomotor nerve, Guillain-Barre syndrome, and Marcus Gunn (jaw-winking) syndrome. This also includes pseudoretraction, which is commonly seen with contralateral blepharoptosis due to overcompensation in accordance with Hering's law.

The third major classification of eyelid retraction, mechanistic etiologies, includes causes related to structural changes in eyelid architecture. This includes congenital, cicatricial, traumatic, neoplastic, or postoperative causes.

Cross-References

- ▶ Graves' Disease
- ▶ Lower Lid Retraction
- ▶ Treatment for Lid Retraction

Further Reading

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Usher Syndrome

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Definition

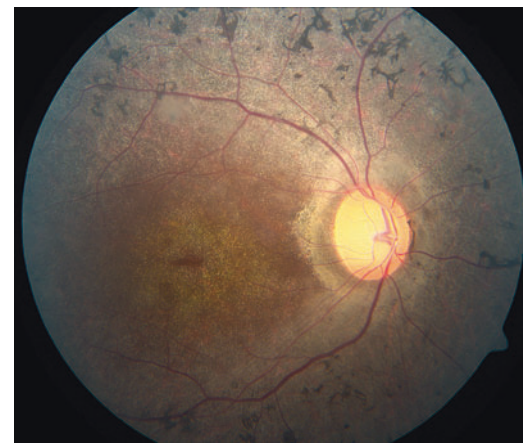
Usher syndrome is an autosomal recessive disease that involves retinal degeneration in combination with sensorineural hearing loss.

Etiology

Etiology of Usher syndrome involves an abnormality in a dynamic protein complex that encodes for axonemal components, which are vital for ciliated structures in both photoreceptor cells of the retina and the hair cells of the inner ear. Multiple subtypes of abnormalities are known, and each can be differentiated according to specific gene and protein involved (Carr and Noble 1999; Gass 1997; Keats 2005; Weleber and Gregory-Evans 2006).

Clinical Presentation

Clinical signs of Usher syndrome involve fundus abnormalities common to other hereditary retinal diseases such as retinitis pigmentosa. These include attenuated retinal arterioles, peripheral pigment clumping, diffuse bone-spicule pigmentation, and waxy pallor of the optic nerve head (Fig. 1). Age of onset and degree of vision loss varies according to class of Usher syndrome. Currently, there are three types of Usher syndrome. Type 1 involves vestibular dysfunction, profound congenital sensorineural hearing loss, and childhood-onset retinopathy. Vestibular dysfunction may be the earliest sign and manifests as delayed walking (mean age of 20 months). Nyctalopia usually develops by 15 years of age. Type 1 patients lose vision quickly with only 77% of patients maintaining a visual acuity of 20/200 by the age of 40 years of age. Type 2 patients demonstrate nonprogressive partial congential



Usher Syndrome, Fig. 1 Color fundus photograph from an individual with Usher syndrome demonstrating typical fundus abnormalities of retinitis pigmentosa

deafness, later-onset mild retinopathy, and no vestibular dysfunction. Over 95% of patients with Type 2 disease maintain a visual acuity of 20/200 at 40 years of age. Type 3 is the least common class of Usher syndrome and is characterized by adult-onset progressive deafness (usually between the ages of 20–40), adult-onset retinopathy, and hyperopic astigmatism. Vestibular deafness and retinal degeneration are variable both in degree and age of onset in Type 3 Usher syndrome.

Diagnostics

Diagnosis of Usher syndrome begins with recognizing symptoms of a retinal degeneration in combination with hearing and vestibular dysfunction. Dilated ophthalmoscopy identifies the typical signs of retinal degeneration, and electroretinogram documents the degree of retinal dysfunction. Classically, the electroretinogram ranges between profoundly abnormal to nondetectable by non-averaging techniques in all types. Formal genetic studies are available to identify specific mutations and type of Usher syndrome. Formal visual field testing is helpful to evaluate degree of peripheral visual field loss and determine need for low vision aids and counseling.

Differential Diagnosis

Differential diagnosis of Usher syndrome includes disease with retinal abnormalities and hearing loss, including congenital rubella, Alport syndrome, Refsum disease, Hurler syndrome, Cockayne syndrome, Bardet-Biedl syndrome, Alstrom disease, Flynn-Aird syndrome, Friedreich ataxia, and Kearns-Sayre syndrome. Distinguishing features include mode of inheritance, prenatal history, spectrum of disease, and physical findings.

Prophylaxis

No prophylaxis is available.

Therapy

Currently, no cure is available for Usher syndrome. Therapy is aimed at maximizing auditory and visual function through the use of auditory and visual aids. For many patients, a team approach utilizing an ophthalmologist, otolaryngologist, audiologist, and social worker is required to help these patients maintain maximal functioning in their tasks of daily living.

Prognosis

Visual prognosis for Usher syndrome varies according to type of disease, but is overall generally poor. Type 1 produces severe progressive vision loss, with age of onset early in childhood. Type 2 disease produces less severe vision loss, with age of onset typically during second decade of life. Type 3 produces the most variable amount of vision loss, with age of onset being quite variable as well.

Epidemiology

Prevalence of Usher syndrome is estimated to be 3 cases per 100,000. Mode of inheritance is autosomal recessive with both sexes being affected equally.

Cross-References

- ▶ Alport Disease/Syndrome, Renal
- ▶ Atypical Retinitis Pigmentosa (RP)
- ▶ Bardet–Biedl Syndrome, Renal
- ▶ Electroretinogram
- ▶ Kearns Syndrome
- ▶ Photoreceptor Cells
- ▶ Retinal Hole
- ▶ Retinitis Pigmentosa, Decreased Vision in Neuro-Ophthalmology

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Uvea (Uveal Tract)

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Synonyms

Uveal Tract

Definition

The uvea is a vascular, pigmented structure of the eye composed of three different parts: the iris, the ciliary body, and the choroid. It lies between the sclera and the neuroepithelium and contains melanocytes that give it its unique color.

Structure

The uvea consists of the iris, the ciliary body, and the choroid.

The iris is a pigmented diaphragm that lies just anterior to the crystalline lens and separates the anterior and posterior parts of the eye. The iris can be divided into three different layers: (1) the anterior border layer that creates the ridges and crypts of the iris surface, (2) the stroma which is the thickest layer and contains blood vessels and nerves, and (3) the posterior layer that consists of the dilator muscle, sphincter muscle, and pigmented epithelium.

The ciliary body adjoins the iris base anteriorly and is continuous with the choroid posteriorly. It can be divided into an anterior ring, the pars plicata, and a posterior ring, the pars plana. The pars plicata contains 70–75 fingerlike projections called the ciliary processes. Ciliary processes have an inner stroma that contains smooth muscle, vascular networks, melanocytes, and connective tissue. The pars plana is approximately 3.5–4.0 mm wide in an adult eye and extends from the pars plicata to the choroid. The ciliary body is covered by a bilayered epithelium. The innermost nonpigmented ciliary epithelium is the main source of aqueous humor in the eye. The zonula occludens of the outer pigmented ciliary epithelium creates the blood-aqueous barrier.

The choroid forms the posterior part of the uveal tract and lies between the sclera and retina and extends from the ora serrata to the optic nerve. The choroid consists of four different layers from anterior to posterior: Bruch's membrane, choriocapillaris, stroma, and suprachoroid. Bruch's membrane has five different layers: the basement membrane of the retinal pigment epithelium (RPE), the inner collagenous zone, an elastic layer, the outer collagenous zone, and the basement membrane of the choriocapillaris. The choriocapillaris is the capillary layer of the choroid and contains fenestrated vessels that provide the blood supply to the RPE and outer retina. The stroma contains larger, unfenestrated vessels, melanocytes, and fibroblasts. The suprachoroid is the outermost layer of the choroid where it adjoins the sclera and is a network of collagen fibers, fibroblasts, elastic fibers, melanocytes, ganglion cells, and nerve complexes.

Function

The uvea serves many functions in the eye. Blood to most of the eye is supplied by the uvea via the anterior and posterior ciliary artery branches of the ophthalmic artery. Dilation and constriction of the pupil result from sympathetic and parasympathetic stimulation of the dilator and sphincter muscles located in the posterior iris. Aqueous humor of the eye is produced by the nonpigmented ciliary body epithelium. Near accommodation is the result of ciliary body smooth muscle contraction which reduces zonular tension on the lens of the eye and shifts it forward. Ciliary body muscle contraction also increases aqueous outflow of the

eye by opening the trabecular meshwork. The choroid plays an important part in heat dissipation in the eye and nourishes the RPE and outer retina.

Clinical Relevance

Inflammatory changes can occur in the uveal tract as a result of infectious, traumatic, neoplastic, or autoimmune insults and result in uveitis. Both primary and metastatic neoplasms of the eye can occur in the iris, ciliary body, and choroid.

Cross-References

- ▶ Accommodation, Functional (Nonorganic/Nonphysiologic) Disorders of
- ▶ Aqueous Humor
- ▶ Choroidal Hemangioma
- ▶ Ciliary Body
- ▶ Iris Deficiency
- ▶ Uveitis, Iridocyclitis

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Uveal Melanoma

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Synonyms

Choroidal and/or ciliary body and/or iris melanoma; Intraocular melanoma; Ocular melanoma

Definition

Uveal melanomas arise from uveal melanocytes distributed throughout the stroma of the choroid, ciliary body, and iris. Malignant melanomas often develop from preexisting nevi.

Etiology

Uveal melanoma's etiology is poorly understood, but risk factors for uveal melanoma include pigmentation factors (light iris and complexion, propensity to sunburn), the presence of cutaneous and iris nevi (Seddon and McCannell 2013), and ocular or oculodermal melanocytosis. Genetic mutations including mutations in GNAQ or GNA11 have been demonstrated in greater than 80% of primary uveal melanomas (Harbour and Chao 2014).

Clinical Presentation

Diagnostics

The diagnosis of uveal melanoma is usually made based upon fundoscopic examination in conjunction with ultrasound and fluorescein angiography. Immediate treatment after diagnosis is routine. Until recently, biopsy was generally not indicated. However, many patients will elect to have a fine needle biopsy after diagnosis for the purpose of molecular prognostic testing, which reliably predicts the risk of metastatic disease.

In the USA, follow-up is completed every six months to annually after local treatment, and typically consists of ophthalmological examination, liver function tests, and/or imaging of the liver with CT scan, MRI, or ultrasound to monitor for metastasis. Although most metastases develop within 3–6 years of diagnosis, late recurrences are not unusual so long-term surveillance is prudent.

Differential Diagnosis

Choroidal nevus, choroidal metastasis, choroidal hemangioma, hemorrhagic RPE, or choroidal detachment.

Prophylaxis

None.

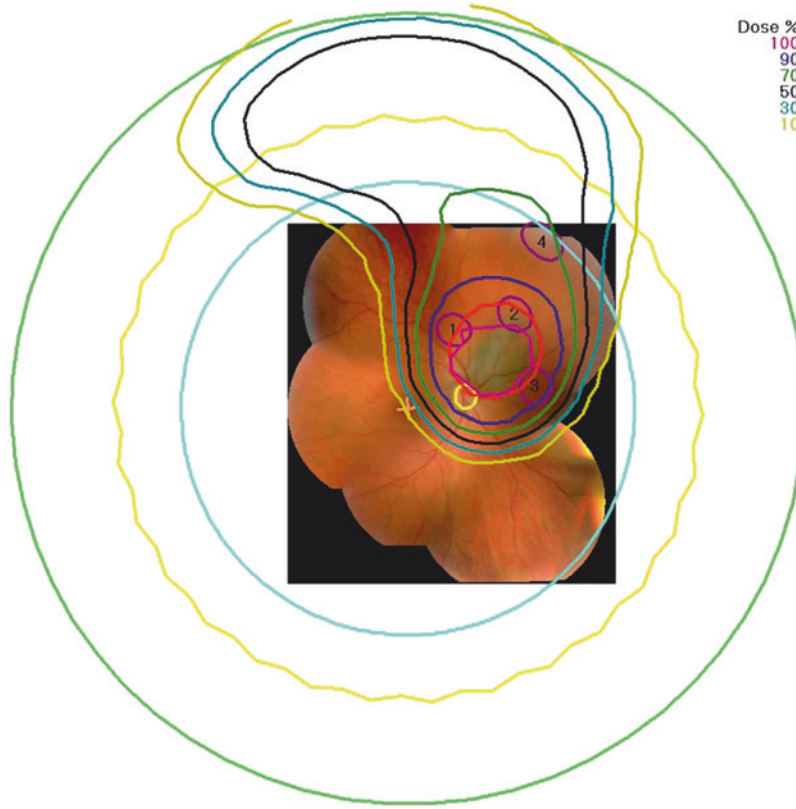
Therapy

Iris melanomas are either excised or treated with radiotherapy. Although some ciliary body melanomas are treated with cyclectomy, the majority of ciliary body melanomas and most choroidal melanomas are treated conservatively with one of two forms of radiotherapy (RT): brachytherapy using radioactive plaques or external beam RT (EBRT). Radiation therapy is hypothesized to cause lethal chromosomal injury to tumor cells. Additionally, it indirectly affects tumor viability by damaging the tumor vasculature that is necessary for tumor growth and systemic tumor cell dissemination. Local tumor control is achieved in nearly all cases, and survival rates are similar to those seen after enucleation.

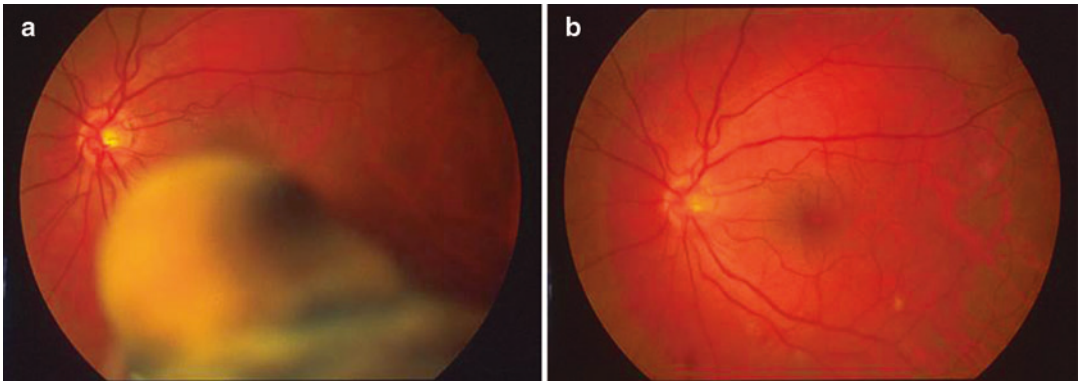
Depending on the clinical characteristics of the tumor, enucleation (very large tumors or cases with large extrascleral extension), resection, and thermotherapy (small tumors or as an adjunct to brachytherapy to reduce risk of tumor recurrence) may be considered as alternative therapies.

Proton Therapy

Charged particle irradiation is the most common type of EBRT. Although several types of charged particles (protons, carbon ions, helium ions) have been used to irradiate uveal tumors, proton irradiation is the only one used today. The highly localized and homogeneous dose distributions achieved with protons allow for the treatment of tumors located near the optic disk and fovea and large tumors, tumors that may be unsuitable for brachytherapy (Gragoudas et al. 2008) (Fig. 1).



Uveal Melanoma, Fig. 1 Proton Irradiation: Treatment Planning. A wide-angle view of the eye shows the position of the tumor (*red contour*), four tantalum markers (*purple ovals*), and the planned isodoses. In the background, a composite small-angle fundus image is registered to the eye model. The displayed eye structures are limbus (*green circle*), ora serrata (*wavy yellow line*), equator (*blue circle*), optic disk (*yellow circle*), and posterior pole (*orange cross*)



Uveal Melanoma, Fig. 2 Tumor Regression. Choroidal melanoma protruding through the vitreous in close proximity to both the optic nerve and macula. (**a**) Before proton irradiation. (**b**) After proton irradiation, tumor has significantly regressed

The tumor is controlled in 95% and the eye is maintained in 84% of patients after proton irradiation (Fig. 2). Approximately one-quarter of patients who undergo enucleation do so because the tumor has recurred (Gragoudas et al. 2002).

As with all types of RT, radiation retinopathy and optic neuropathy can develop after proton irradiation. For patients who have tumors located near the fovea or optic disk, some radiation exposure is inevitable, and the risk of radiation maculopathy, radiation papillopathy, and vision loss as a secondary complication is increased. Reported 5-year rates of maculopathy, papillopathy, and vision loss after proton irradiation in patients with tumors located in close proximity to these critical structures were 64%, 35%, and 68%, respectively (Lane and Gragoudas 2007).

Other complications that may significantly affect visual function include cataracts, neovascular glaucoma, and vitreous hemorrhage.

Prognosis

Iris melanomas have a more benign course than ciliary body and choroidal melanomas (10-year survival is approximately 95% for iris tumors compared to 77% for choroidal tumors). Survival rates are lower in patients who possess high-risk characteristics such as large tumor size, heavily pigmented tumors, or tumors originating in the ciliary body. Molecular prognostic testing with gene expression profiling or DNA analysis is now available and can accurately classify patients as having low or high risk of disease progression (Damato et al. 2007; Cassoux et al. 2014; Ganguly et al. 2014; Harbour and Chao 2014).

The 15-year cumulative probability of dying from metastasis, calculated using risk scores derived from logistic regression models of clinical prognostic factors, illustrate the variation in risk: the melanoma-related mortality rate was less than 10% in the group of patients with the lowest risk scores compared to over 50% in the highest risk score patient group (Gragoudas et al. 2002).

For patients who develop metastatic disease, the prognosis is poor. Effective treatments for hepatic metastasis, the most common site in uveal melanoma, are lacking. Nevertheless, more frequent monitoring of patients at high risk may be worthwhile so that patients can be referred for palliative care or experimental therapies.

Epidemiology

Uveal melanoma is rare, with an incidence of five cases per million annually in the USA. Approximately 95% of ocular melanomas arise in the uvea, and the most common location is the

choroid (more than 80% of cases). Uveal melanoma is the only life-threatening tumor of the eye in adults. It is more common in males than females and develops predominantly in white populations (Seddon and McCannell 2013).

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Uveal Tract

► Uvea (Uveal Tract)

Uveitic Glaucoma

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Synonyms

Secondary glaucoma in uveitis/inflammatory eye disease

Definition

Intraocular pressure (IOP) rise due to intraocular inflammation with associated optic nerve damage.

Etiology

Three possible mechanisms are involved in the pathogenesis of inflammatory hypertension or glaucoma adapted from (Radhakrishnan et al. 2010):

1. Direct inflammation of the trabecular meshwork or trabeculitis (IOP elevation parallels inflammatory activity)
2. Acute angle closure due to inflammatory changes
   1. Pupillary block (iris bombé caused by posterior synechiae)
   2. Non-pupillary block (forward movement of the lens-iris diaphragm due to ciliochoroidal effusion)
3. Chronic, mixed-mechanism ocular hypertension/glaucoma
   1. Chronic closed angle (anterior synechiae or vascular membranes)
   2. Open angle (increased outflow resistance due to chronic damage in the trabecular meshwork)

Friederike Mackensen: deceased.

Clinical Presentation (Listed by Supposed Etiology)

1. See other uveitis etiologies and Posner-Schlossman syndrome:
   1. Fibrinous uveitis forms such as acute anterior uveitis with HLA-B27
   2. Vogt-Koyanagi-Harada syndrome, scleritis, and sympathetic ophthalmia
2. For example, anterior uveitis associated to juvenile idiopathic arthritis (JIA), sarcoidosis, and Fuchs uveitis syndrome (FUS).

Diagnosis

The most important diagnostic tool is correct determination of IOP at each visit regardless of patient age or emergency setting. Goldmann applanation measurements are still the gold standard; in some patients which cannot be examined on the slit lamp, handheld tonometers can be helpful. Appropriate diagnostic steps when glaucoma is suspected: visual field examination and morphometric examination of the optic nerve head.

Differential Diagnosis

Inflammatory ocular hypertension syndromes not leading to optic nerve damage. Entities where noninflammatory materials block the trabecular pores, as, for example, lens material in phacolytic glaucoma or red blood cells in hyphema. Distinction of pupillary and non-pupillary block should usually be feasible by slit lamp exam; in some cases ultrasound biomicroscopy may be helpful. An important differential diagnosis is corticosteroid-induced IOP rise or glaucoma which may occur days to weeks after initiation of treatment. Therefore, it is of utmost importance to check the IOP of uveitis patients at the first visit!

Prophylaxis

To avoid scarring of trabecular meshwork, strict uveitis control is advisable. Patient counseling about the importance of regular medication. Visual field examination and morphometric examination of the optic nerve head should be repeated in regular intervals to monitor the treatment effect.

Therapy

Uveitis should be treated according to the suspected underlying mechanism and/or anatomic presentation. When in doubt regarding a potential role for corticosteroids in pressure rise, loteprednol may be an alternative or corticosteroid-sparing medication altogether. Care should be taken not to undertreat uveitis for the fear of corticosteroid-related side effects as then complications of chronic inflammation may develop. Antiglaucomatous medication can be chosen similar to treatment of POAG, except that prostaglandin analog should be reserved for third-line treatment as they may promote inflammation or macular edema. Still a small clinical trial found no disadvantage of a prostaglandin analog therapy (Markomichelakis et al. 2009) and better IOP control. So first beta-blockers (cave lung disease in sarcoidosis) and then carbo-anhydrase inhibitors followed by alpha agonists or prostaglandin analog should be used (Radhakrishnan et al. 2010). In cases of acute angle closure, laser peripheral iridotomy is the treatment of choice. In angle closure due to choroidal effusion, systemic corticosteroids and cycloplegia are indicated. In cases of chronic glaucoma, surgical treatment may be needed. Trabeculectomy with mitomycin C reaches similar success rates to POAG eyes (Kaburaki et al. 2009). In failures a filtering implant should be considered. Uveitis has to be controlled medically before surgical treatment can be done.

Prognosis

The prognosis of uveitic glaucoma depends on the complications already having taken place.

Epidemiology

Generally the incidence of chronic uveitic glaucoma is low, ranging in sarcoidosis-associated uveitis from 11 to 26%, in FUS up to 60%, and 6 to 8% in JIA-associated anterior uveitis (Heiligenhaus et al. 2007).

Cross-References

- Fuchs Heterochromic Iridocyclitis, Glaucoma
- Fuchs' Uveitis Syndrome (FUS) with Secondary Glaucoma
- Other Uveitic Etiologies
- Traumatic Glaucoma
- Uveal Melanoma

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Uveitis in Multiple Sclerosis

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Synonyms

MS-associated uveitis

Definition

The uvea is the middle layer of the eye, divided anteriorly into the iris and ciliary body and posteriorly into the choroid. Inflammation of the anterior uveal tract is known as anterior uveitis or iritis. Uveitis posterior to the lens includes vitritis, intermediate uveitis, pars planitis (accumulation of yellow-gray inflammatory exudates at the pars plana and ora serrata), choroiditis, retinitis, chorioretinitis, and retinochoroiditis.

Simultaneous inflammation anterior and posterior to the lens is known as panuveitis.

Etiology

Though the etiology of multiple sclerosis (MS)-associated uveitis is not yet completely understood, the possibility of a genetic component is substantiated by the presence of a shared human leukocyte antigen (HLA). MS is associated with *HLA-DR2*, found in 50–70% of North American and European patients compared with 20–25% of controls, and the same *HLA-DR2* antigen has also been associated with intermediate uveitis. Malinowski et al. reported a positive *HLA-DR2* in 67.5% of 40 patients with pars planitis, compared with 28% of controls. Within this specific cohort, MS subsequently developed in 12.5%. The results of this study along with several others suggest an immunogenetic predisposition to pars planitis, MS, and MS-associated uveitis; however the relationship between *HLA* modulation and the pathogenesis of inflammation in both the eye and the central nervous system (CNS) remains ambiguous.

Though the association between MS and uveitis is well documented and has been reported since 1947, with the majority of descriptions being based on patients with pars planitis, the pathophysiological connection between MS and uveitis is unknown. Some have speculated that a process similar to the autoimmune demyelinating manifestations of MS occurs in the eyes of patients with MS-associated uveitis; however, certain inflammatory types occur in locations with no myelin present. Other theories have postulated a common, nonmyelin antigen in the CNS and the retina and/or uvea as the target of the inflammatory response, such as in the mouse model of MS where passively transferred autoreactive T cells against astrocyte-derived protein S100B stimulate both CNS inflammation and uveitis. In a larger study of 93 autopsied eyes in patients with MS, 7 eyes had lymphocytic or granulomatous retinal periphlebitis and 5 eyes had focal areas of lymphocytic or granulomatous retinitis. 44.7% had optic nerve atrophy, including all eyes with active ocular inflammation. Immunoperoxidase studies of the retinal veins showed a pervasive distribution not confined to areas with focal periphlebitis lesions. The authors thus concluded that this nonspecific inflammation was the result of the autoimmune response, though it is still unknown whether the inflammation is due to a primary vasculitis versus a secondary response against an unknown antigen.

Clinical Presentation

The most common type of MS-associated uveitis is intermediate uveitis (pars planitis), defined as inflammation predominantly of the vitreous cavity, though this prevalence varies. Additionally, a myriad of nonspecific clinical features have been reported, with early reports of uveitis in patients with MS highlighting retinal periphlebitis in association with vitreous inflammation and retinal edema. Significantly, not all patients with MS-associated uveitis present clinically with intermediate uveitis, and patients with MS have been reported to have all types of uveitis (anterior, intermediate, and posterior), as well as cataract, macular edema, and epiretinal membrane formation. A study examining both the clinical and radiological characteristics of patients with MS and coexisting uveitis noted no correlation between the type of uveitis and the type of MS, consequently concluding that patients with MS and coexisting uveitis have a clinical pattern no different than "typical" MS.

Diagnostics

Cranial magnetic resonance imaging (MRI) is the test of choice to support the clinical diagnosis of MS, but some patients require ancillary testing to support the diagnosis including lumbar

puncture (showing IgG abnormalities or oligoclonal bands).

Differential Diagnosis

Behcet disease
Syphilis
Sarcoidosis

Other infections (e.g., Lyme borreliosis, toxocariasis, tuberculosis, cat scratch disease, and West Nile viral infection)

Therapy

Treatment of MS-associated uveitis depends on both the location and degree of inflammation. For instance, intermediate uveitis may require no treatment when vision-threatening complications (e.g., macular edema) are absent due to the fact that the risk of therapy may outweigh the benefits. It is still unknown whether early treatment of MS-associated uveitis in patients who do not have vision compromise has any long-term benefit with regard to vision or MS itself. Similar to other types of uveitis, treatment options include topical, oral, periocular, and intravitreal steroids, in addition to immunosuppressants. In those patients who have snowbanking and in whom systemic or periocular steroids have been ineffective, cryotherapy to the retinal periphery has been employed. Likewise, laser photocoagulation has also been used in patients with pars planitis. These treatments carry the risk of augmenting inflammation and higher risk of rhegmatogenous retinal detachments.

One possible beneficial treatment option is the use of interferons (IFN). IFN-β has been used to alleviate the frequency and severity of MS flares and has also been shown to decrease ocular inflammation in experimental autoimmune encephalomyelitis. One small study of 13 patients examined this treatment in MS-associated uveitis and had visual acuity improve in 17 eyes (71%) during a median follow-up time of 24.6 months. The results are promising, but additional studies are needed.

Prognosis

Long-term visual outcomes and complications were examined in a study by Malinowski in patients with pars planitis and overall showed favorable prognoses. Patients that had significant cataracts appeared to have greater risks for retinal detachments. Periphlebitis at the time of pars planitis diagnosis increased the risk for future development of optic neuritis or MS.

The prognosis of MS-associated uveitis is dependent on the MS subtype and the severity of the uveitis. The relapsing-remitting form of MS is generally associated with a better prognosis than progressive disease. In those whom have the progressive form from the onset, irreversible disability occurred sooner when compared with those with the relapsing-remitting onset. In patients with the new-onset anterior uveitis, factors associated with a lower rate of treatment-free remission and persistent inflammation include bilateral uveitis and presentation with 1+ or more vitreous cells or visual acuity of 20/200 or worse.

Epidemiology

The incidence of MS-associated uveitis has wide variability and depends on numerous factors, including the patient population, type of uveitis, and diagnostic criteria for both MS and uveitis. Uveitis is significantly more common in patients suffering from MS, with some data reporting up to ten times the frequency encountered in the general population. Likewise, the frequency of MS in patients with uveitis is 0.5–14%, versus 0.02–0.12% found in the general population. Demographically, MS-associated uveitis is frequently bilateral, presenting in individuals between 20 and 50 years of age, with two of the larger pars planitis studies reporting a mean age of onset of uveitis reported between 22.4 and 22.6 years of age. These patients are frequently

female, which is in accordance with the female prevalence in MS and most forms of uveitis.

Cross-References

► Retinitis Pigmentosa, Decreased Vision in Neuro-Ophthalmology

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Uveitis, Iridocyclitis

► Fuchs Heterochromic Iridocyclitis, Glaucoma

Uveoparotid Fever

► Heerfordt's Syndrome

V

V1

► V1 (Ophthalmic Nerve)

V1 (Ophthalmic Nerve)

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Synonyms

Ophthalmic division of the trigeminal nerve; Ophthalmic nerve; V1

Definition

The ophthalmic nerve (*V1*) or ophthalmic division of the trigeminal nerve contains afferent sensory fibers to the skin overlying the frontal and nasal bones. Similarly, the sensation to the cornea and the conjunctiva is supplied by V1.

Once the ophthalmic division of the trigeminal nerve comes off the trigeminal ganglion, V1 enters the cavernous sinus along with the maxillary division (V2); cranial nerves III, IV, and VI; and the internal carotid artery. Ocular sympathetic fibers on the internal carotid artery join the ophthalmic division within the cavernous sinus. After exiting the cavernous sinus, yet before entering the superior orbital fissure, the ophthalmic division splits into three separate branches: the lacrimal, frontal, and nasociliary nerves.

The lacrimal nerve goes to innervate the lacrimal gland after receiving autonomic fibers necessary for this gland's function. Autonomic fibers travel with the lacrimal nerve via a communicating branch of the zygomaticotemporal nerve and are responsible for lacrimal gland function. The lacrimal nerve supplies sensory fibers to parts of the lid and conjunctiva. The frontal nerve divides into the supraorbital nerve and supratrochlear nerves which provide sensory input to the upper eyelid, scalp, and forehead.

The nasociliary nerve provides sensory innervation to the globe and cornea through many

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branches. A terminal branch of the nasociliary nerve, named the external nasal nerve, provides sensory input to the nose and may become involved in herpes zoster ophthalmicus (i.e., the shingles). When the tip of the nose is involved with herpes zoster virus (HZV), it has been referred to as the Hutchinson sign and may have prognostic importance for the development of ocular involvement. The long ciliary nerve (a branch of the nasociliary nerve) is also of interest as it does not synapse in the ciliary ganglia, yet serves to bring postganglionic sympathetic nerve fibers into the ciliary ganglion. These long ciliary nerve fibers are joined by postganglionic parasympathetic fibers and continue as short ciliary nerves. Sympathetic fibers from the long ciliary nerves innervate the dilatory pupillae muscle, whereas afferent sensory fibers travel though the ciliary ganglion to innervate the cornea and eyeball.

Cross-References

- ▶ Lacrimal Nerve
- ▶ V2 (Maxillary Nerve)
- ▶ V3 (Mandibular Nerve)

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V2

- ▶ V2 (Maxillary Nerve)
- ▶ V3 (Mandibular Nerve)

V2 (Maxillary Nerve)

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Synonyms

Maxillary division of the trigeminal nerve; Maxillary nerve; V2

Definition

The maxillary nerve (*V2*) provides sensory input to the conjunctiva, eyelid, and skin overlying the maxillary and zygomatic bones. Once the maxillary division of the trigeminal nerve comes off the trigeminal ganglion, V2 enters the posterior cavernous sinus along with cranial

nerves III, IV, V1, and VI, the ocular sympathetic fibers, and the internal carotid artery. After leaving the cavernous sinus, the maxillary division does not enter the superior orbital fissure. Instead, V2 exits the skull base via the foramen rotundum. Traveling anteriorly, the maxillary nerve sends a branch to the pterygopalatine ganglia but continues forward. Unlike cranial nerves V1, III, IV, and VI, the maxillary division enters the orbit through the inferior orbital fissure.

The zygomatic nerve splits into the zygomaticofacial and zygomaticotemporal nerves. The zygomaticofacial nerve is responsible for sensation of the cheek, while the zygomaticotemporal nerve is responsible for sensation in the temporal region. It is worth noting the zygomaticotemporal nerve sends a communicating branch to the lacrimal nerve carrying parasympathetic nerves to the lacrimal gland. After the zygomatic nerve branches off, the maxillary nerve continues and becomes the infraorbital nerve and travels through the inferior orbital fissure. The infraorbital nerve then branches several times to supply sensory input to the conjunctiva and skin of the inferior eyelid.

Cross-References

- ▶ Lacrimal Nerve
- ▶ V1 (Ophthalmic Nerve)
- ▶ V3 (Mandibular Nerve)

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V3 (Mandibular Nerve)

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Synonyms

Mandibular division of the trigeminal nerve; Mandibular nerve; V2

Definition

The mandibular nerve (*V3*) provides sensation to the mandibular prominence and motor innervation to the muscles of mastication. Once the mandibular division (V3) of the trigeminal nerve comes off the trigeminal ganglion, V3 does not enter the cavernous sinus like the other two divisions of the trigeminal nerves (V1 and V2). Instead, motor fibers join the mandibular division

and V3 exits the calvarium through the oval-shaped canal named the foramen ovale.

After giving off the meningeal branch, the mandibular nerve splits into a posterior division and an anterior division. Eventually, these branches innervate the muscles of mastication and sensation to the mandibular prominence. Cutaneous sensory nerves that branch from the third division of the trigeminal nerve include the buccal, auriculotemporal, and mental nerves.

Cross-References

- ▶ V1 (Ophthalmic Nerve)
- ▶ V2 (Maxillary Nerve)

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Valerio's Mosaic Degeneration

- ▶ Shagreen, Crocodile

Valve of Hanske

- ▶ Rosenmüller, Valve of

Varicella Zoster Virus

- ▶ Herpes Zoster Ophthalmicus

Varices, Orbital

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Synonyms

Type-II vascular malformation

Basic Characteristics

Definition

Orbital varices are a rare orbital vascular malformation, representing abnormally dilated orbital veins. Most commonly orbital varices involve the superior ophthalmic vein, although any orbital vein may be involved. Orbital varices account for approximately 1% of orbital tumors in histopathologic series (Karcioglu 2014).

Etiology

Congenital or acquired weakening of the vein wall leads to the development of orbital varices. Factors contributing to vessel weakening are poorly understood.

These varices are predisposed to thrombosis, owing to sluggish blood flow through the weakened vessel as well as pooling of blood. Orbital veins are valveless, increasing the tendency of blood to pool in these veins. When thrombosis occurs and further obstructs blood flow, there can be proximal distention and enlargement of the varix (Karcioglu 2014).

Clinical Features

Demographics

Orbital varices typically present in the second to fourth decade, although they may be present in any age group. Orbital varices are rare and comprise between 0% and 1.3% of orbital tumors (Karcioglu 2014).

Signs and Symptoms

Patients with orbital varices typically present with painless intermittent proptosis. Proptosis is often only present or exacerbated during activities that increase central venous pressure, such as coughing, straining, bending, prone positioning, and the Valsalva maneuver. Positional proptosis occurs because the varix is in communication with the systemic venous circulation and may not be seen in patients with non-distensible varices (Karcioglu 2014). Other clinical signs and symptoms may include widening of the palpebral fissure, eyelid ptosis, and even irregular astigmatism or optic nerve compression depending on the location of the lesion. Rarely, orbital varices may present acutely with sudden onset pain and proptosis as a result of hemorrhage or thrombosis. Hemorrhage into an orbital varix may cause an orbital compartment syndrome with pain, proptosis, and optic nerve compromise.

Categorization

Venous malformations are defined by the degree of vascular flow. Type-I lesions have no flow, Type-II lesions have slow venous flow, and Type-III lesions have rapid, arterial-type flow. Orbital varices are categorized as Type-II venous malformations with low-pressure flow through dilated venous channels.

Orbital varices are described as distensible or non-distensible. Varices are typically distensible, owing to the weakened vessel wall. Non-distensible lesions may not demonstrate the classic positional proptosis and are more likely to hemorrhage than distensible varices (Black and Smith 2012).

Orbital varices may be further classified as primary or secondary lesions. A primary orbital varix is an isolated lesion that is confined to the orbit and is not associated with any other pathology. In contrast, a secondary orbital varix develops as a consequence of an intracranial arteriovenous malformation shunting blood into the orbital veins and causing them to dilate (Karcioglu 2014).

Differential Diagnosis

The differential diagnosis for unilateral proptosis includes lymphangioma, capillary hemangioma, arteriovenous fistula, hemorrhage, trauma, thyroid eye disease, idiopathic orbital inflammation (orbital pseudotumor), lymphoma, and metastatic disease. The differential for spontaneous orbital hemorrhage includes lymphangioma, trauma, bleeding disorder, and cavernous hemangioma (Karcioglu 2010).

Diagnostic Workup

Clinical Evaluation

Patients with suspected orbital varices should undergo a complete ophthalmic examination including exophthalmometry to assess for proptosis. Exophthalmometry should be performed with the patient relaxed and then repeated with patient performing the Valsalva maneuver. Dynamic proptosis that increases with Valsalva suggests an orbital varix.

Imaging

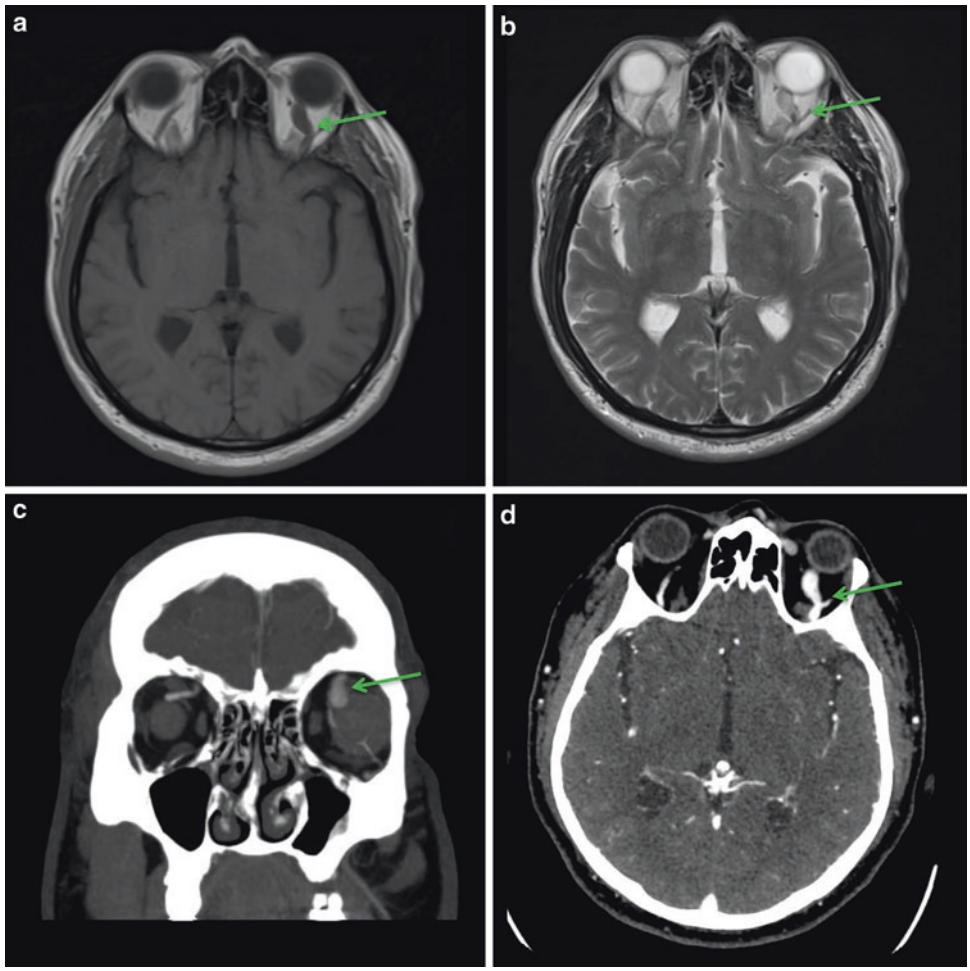
Multiple imaging modalities are available for the diagnosis and evaluation of orbital varices. The traditional "gold standard" for vascular malformations is digital subtraction angiography. However, catheter angiography carries a risk of stroke or vascular compromise to the eye and is difficult to perform given the small caliber of orbital vessels. In addition, catheter angiography does not provide visualization of surrounding orbital structures and has largely been replaced by noninvasive modalities including ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) (Black and Smith 2012). Brain imaging should also be performed as approximately 10% of patients have a non-contiguous intracranial vascular malformation (Karcioglu 2010).

Ultrasound On ultrasound imaging, orbital varices appear as dark, anechoic tubes. On A-scan ultrasound, varices demonstrate low internal reflectivity and expansion of the lesion with Valsalva. On B-scan ultrasound, varices appear as linear, channeled structures with an echolucent lumen. Color Doppler imaging may be utilized to observe venous flow and typically demonstrates dynamic change in the lesion size during

respiration and increased venous flow or flow reversal with the Valsalva maneuver (Karcioglu 2010).

Computed Tomography (CT) CT is noninvasive and provides excellent visualization of orbital structures. CT is relatively inexpensive and can be obtained rapidly but exposes the patient to radiation. CT angiography may be performed with the aid of iodinated contrast media, although caution must be exercised as some patients have a serious allergy to contrast. On CT, orbital varices appear as a dilated, tortuous vessel that tapers towards the orbital apex (Esmaeli 2010). CT is excellent at demonstrating phleboliths, which appear hyperintense. Dynamic CT and CTA can be performed with the patient performing the Valsalva maneuver and demonstrate enlargement of the lesion and changes in blood flow.

Magnetic Resonance Imaging (MRI) Similar to CT, MRI provides high-quality noninvasive imaging. MRI does not involve any radiation



Varices, Orbital, Fig. 1 Imaging characteristics of orbital varices. Imaging from patient with an incidentally discovered varix of the Left superior ophthalmic vein. **a** Axial T1 MRI demonstrating hypointense varix. **b** Axial T2 MRI with hyperintense varix. **c** Coronal CTA demonstrating contrast filling of dilated vein. **d** Axial CTA demonstrating contrast filling of dilated vein

exposure and carries a smaller risk of contrast allergy but is more expensive and takes longer to obtain relative to CT imaging. Similar to CT, MRI demonstrates a dilated, tortuous varix that expands with Valsalva. Orbital varices range from hypointense to hyperintense on T1 sequences, appear hyperintense on T2 imaging, and demonstrate avid enhancement with gadolinium contrast (Black and Smith 2012) (Fig. 1).

Histopathology

On histopathologic examination, excised varices appear as dilated vascular channels lined by endothelial cells. The vessel walls are line with irregular, attenuated smooth muscle cells (Black and Smith 2012). There is thickening and fibrosis of the vessels walls, and these become lined with hemosiderin pigment as a result of chronic hemorrhage and fibrosis. Pathologic section may also demonstrate chronic infiltration of inflammatory cells as well as intraluminal calcifications consistent with phleboliths (Karcioglu 2014).

Management

Orbital varices are challenging to remove surgically and they are often monitored or managed conservatively. If orbital varices become symptomatic, the anterior portion may be resected or embolization may be attempted (Karcioglu 2010). Resection remains a challenge owing to the confined space of the orbit, proximity to vital structures, and risk of compartment syndrome from hemorrhage and requires an excellent understanding of the surgical anatomy, careful dissection, and hemostasis.

Alternatively, endovascular catheter embolization may be attempted prior to surgery or instead of surgery. Embolization may obviate the need for surgery or decrease the risk of bleeding intraoperatively but requires a skilled interventional radiologist who is familiar with the orbital vasculature. Percutaneous injection of n-butyl cyanoacrylate (NBCA) has also been reported as a preoperative measure to decrease bleeding from orbital varices (Karcioglu 2014).

Cross-References

- ▶ Benign Anisocoria
- ▶ Ultrasound

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Varix

- ▶ Vascular Tumors Disease of the Conjunctiva

Vascular Nevus

- ▶ Port-Wine Stain (Nevus Flammeus)

Vascular System of Orbit

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Function

The ophthalmic artery is the primary source of blood supply to the orbit and is the first branch off the internal carotid artery within the skull. The branches of the ophthalmic artery can be divided into those that will supply the orbit and those supplying the globe.

Arterial Supply to the Globe

The central retinal artery is a branch off the posterior 1/3 of the ophthalmic artery which enters the dural sheath of the optic nerve 13 mm posterior to the globe. The central retinal artery supplies blood to the inner 2/3 of the retina and all the nerve fibers exiting the globe to deliver visual information to the thalamus.

The posterior ciliary arteries branch off the ophthalmic artery soon after the central retinal artery and produce the long posterior ciliary arteries that supply the anterior segment as well as the short posterior ciliary arteries that supply the choroid. There are 6–12 short posterior ciliary arteries that pierce the sclera to enter the globe around the exit site of the optic nerve; these supply the choroid from the posterior pole to the equator of the eye in addition to the ciliary processes. The short posterior ciliary arteries form an anastomotic network that provides the principle blood supply of the optic nerve head, known as the Circle of Zinn-Haller (Hayreh 2006).

There are two long posterior ciliary arteries in each eye that pierce the sclera posteriorly and course anteriorly between the sclera and choroid, each dividing into two branches, until they arrive at the ciliary muscle. There, they form an anastomotic circle around the circumference of the iris, known as the circulus arteriosus major, which connects via multiple branches to another arterial circle at the pupillary margin and also collateralizes with the vascular supply of the extraocular muscles. Thus, the long posterior ciliary arteries supply the choroid, ciliary body, iris.

Arterial supply to the extraocular muscles comes from the muscular branches of the ophthalmic artery, the lacrimal artery, and the infraorbital artery. The muscular artery divides into superior and inferior branches that subsequently give off the anterior ciliary arteries to supply the extraocular muscles. The superior branch supplies the levator palpebral muscle, superior rectus, superior oblique, and a portion of the lateral rectus. The inferior branch supplies the medial rectus, inferior rectus, and inferior oblique. The anterior ciliary arteries move anteriorly along the extraocular muscles to supply the rectus muscles, conjunctiva, and sclera. They then join the long posterior ciliary arteries in forming the major arterial circle of the ciliary body, the circulus arteriosus major. The superior, inferior, and medial extraocular muscles have two anterior ciliary arteries each, while the lateral rectus has only one.

The infraorbital artery is a branch off the maxillary artery that courses with the infraorbital nerve in the infraorbital groove before entering the infraorbital canal which exits onto the surface of the maxilla via the infraorbital foramen. While in the canal, the infraorbital artery gives off branches to supply the inferior rectus, inferior oblique, and the lacrimal sac.

The lacrimal artery commonly branches off the ophthalmic artery before entering the orbit. It joins the lacrimal nerve as it runs along the lateral wall of the orbit at the upper border of the lateral rectus to supply the lacrimal gland, eyelids, and conjunctiva. Along its course, it produces minor branches to supply the superior and lateral rectus muscles.

Arterial Supply to the Orbit

The arterial supply of the eyelids consists of anastomoses between the external carotid artery, which supplies the face, and the internal carotid artery via the ophthalmic artery. As previously mentioned, the lacrimal artery derives from the ophthalmic artery, and its terminal branches include the superior and inferior lateral palpebral arteries that supply the lateral upper and lower eyelids, respectively, as well as the conjunctiva (Foster et al. 2015). The terminal branches of the internal (medial) palpebral artery, also a branch off the ophthalmic artery, include the superior and inferior medial palpebral arteries that supply the lacrimal sac and medial eyelids. The medial and lateral palpebral arteries form anastomotic arches on both the upper and lower eyelid that lie either between the orbicularis oculi and the tarsi or within the tarsus. The upper eyelid has two such arches: one, known as the superior peripheral arterial arcade, is located peripherally at the margin of the tarsal plate within the superior tarsal muscle (Müller's muscle); the second, is the superior marginal arterial arcade that is located 3 mm from the free border of the eyelid. The lower eyelid has a single anastomotic arch, the inferior

marginal arterial arcade. Anastomoses also exist between the lower eyelid circulation and the transverse facial artery and its derivative, the angular artery, which are branches of the external carotid artery. The angular artery extends up to the lateral aspect of the nose and serves as an important landmark in dacryocystorhinostomy.

The supraorbital artery supplies the superior rectus and levator palpebral muscles, before passing though the supraorbital foramen to supply the eyebrow and forehead on the facial surface. The frontal artery leaves the orbit medially to supply the forehead and scalp, where it anastomoses with the terminal branches of the supraorbital artery.

Vascular supply to the sinuses includes the anterior ethmoidal artery, which supplies the superior oblique muscle, anterior and middle ethmoidal cells, frontal sinus, lateral wall nose, and nasal septum. The posterior ethmoidal artery passes through the posterior ethmoidal canal to supply the posterior ethmoidal cells, while the nasal artery supplies the superior lacrimal sac and nose.

Venous Drainage

The venous drainage of the eye consists of two routes classified by their anatomic location relative to the tarsus – pretarsal (superficial) veins drain into the internal and external jugular veins while the posttarsal (deep) veins drain into the cavernous sinus. The superior ophthalmic vein is the primary conduit for venous drainage from the orbit and originates in the superonasal quadrant (Black et al. 2012). The orbital veins are responsible for draining the choroid and include 4–8 vortex veins per eye that exit posterior to the equator with a distribution of 1–2 per quadrant. The 2–4 superior vortex veins merge into the superior ophthalmic vein that exits via the superior orbital fissure into the cavernous sinus. The inferior vortex veins merge to form the inferior ophthalmic vein and exit via the inferior orbital fissure.

The central retinal vein drains blood from the retinal capillaries and is relatively short, running through the optic nerve until about 10 mm posterior to the globe and empties into cavernous sinus, either directly or indirectly through the superior or inferior ophthalmic vein.

Clinical Relevance

The clinical significance of these vascular territories is highlighted during vaso-occlusive events. In particular, the central retinal artery and its branches do not supply the fovea, which is typically sustained by the choroid. In cases of central retinal artery occlusion, a "cherry red spot" is seen as the macula maintains choroidal perfusion amidst a pale, ischemic retina. In some individuals (approximately 20% of the population), a branch of the ciliary circulation known as the cilioretinal artery supplies the retina between the macula and the optic nerve, which allows for preserved central vision even in a central retinal artery occlusion. However, the cilioretinal artery itself is a branch of the short posterior ciliary arteries derived from the ophthalmic artery; therefore, if the cilioretinal artery were to become occluded, significant central vision acuity would be lost despite an intact peripheral visual field (Hayreh 2006). Similar to the central retinal artery, the central retinal vein can suffer from occlusive events.

In addition, the interplay between orbital and ocular vasculature is highlighted during strabismus surgery where detaching the extraocular muscles reduces blood supply to the anterior chamber. For this reason, it is generally preferred to operate on no more than two recti muscles to avoid anterior ischemic syndrome. Resecting or recessing the lateral rectus is generally less significant because of its single arterial contribution to the anterior chamber.

Cross-References

- ▶ Cavernous Sinus Anatomy
- ▶ Ophthalmic Nerve
- ▶ Superior Ophthalmic Vein Thrombophlebitis
- ▶ Vortex Keratopathy

V

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Vascular Tumors Disease of the Conjunctiva

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Synonyms

Acquired sessile hemangioma; Capillary hemangioma; Cavernous hemangioma; Glomangioma; Hemangiopericytoma; Kaposi sarcoma; Lymphangiectasia; Lymphangioma; Pyogenic granuloma; Racemose hemangioma; Varix

Definition

Benign or malignant proliferation of blood vessel endothelium that originates in either conjunctival epithelium or stroma.

Etiology

Most vascular tumors of the conjunctiva occur spontaneously (Shields et al. 2004). Kaposi sarcoma is associated with human herpesvirus 8 infection and almost exclusively seen in patients with acquired immune deficiency syndrome (Hiatt et al. 2008). Pyogenic granulomas are associated with infectious, inflammatory, or traumatic inciting events.

Clinical Presentation

Conjunctival vascular tumors are a heterogenous group of tumors with morphology dependent on the underlying cause of the tumor. The tumors can be divided into benign or malignant tumors.

A lymphangioma is a benign tumor. It can be diffused or circumscribed and generally presents as a soft, red mass with lymphatic vessels. It can present with focal or diffuse hemorrhage and can be confined to the conjunctiva or extend into orbit. Lymphangiomas usually present at birth and enlarge slowly. They are classically described as chocolate cysts (Shields et al. 2011a).

Lymphangiectasias presents as clear or blood-filled linear lymphatic channels. There generally is not a distinct mass.

A pyogenic granuloma is a slowly growing elevated, smooth, red vascular mass. It can be anywhere from sessile with a broad base to a pedunculated mass.

Capillary hemangiomas present in infancy. They are either diffuse or circumscribed with a pink to red appearance. They can enlarge over several months but usually regress without treatment.

A varix is a dilation of thin wall segments of a vein that is missing an elastic layer. It is similar to a lymphangioma in appearance.

Cavernous hemangiomas are red or blue, multiloculated lesions in conjunctival stroma. They can be small and circumscribed or large and diffuse. There is generally a solitary lesion. Diffuse hemangiomatosis of palpebral conjunctiva is indicative of orbital cavernous hemangioma (Shields et al. 2011a).

Racemose hemangioma is a prominent arteriovenous communication in the conjunctiva. The lesions are red and multilobular.

Acquired sessile hemangioma is a recently described sessile mass of curvilinear blood vessels with an associated feeding artery and draining vein. They can regress spontaneously (Shields et al. 2011b).

A glomangioma is a red-blue mass that originates from the glomus body. It is similar in appearance to lymphangioma lesions or cavernous hemangiomas.

Hemangiopericytomas are red conjunctival masses originating from conjunctival stroma. They have both benign and malignant cytological features.

Kaposi sarcoma is a malignant tumor associated with human herpesvirus 8 (HHV-8). It is classically seen in patients with AIDS. It presents as red, diffuse, or multifocal nodular lesions. Sometimes it may look like a subconjunctival hemorrhage.

Diagnosis

Diagnosis is mainly dependent upon clinical examination of the tumor, but definitive diagnosis requires pathologic tissue examination following biopsy.

Differential Diagnosis

Lymphangioma, lymphangiectasia, pyogenic granuloma, capillary hemangioma, Kaposi sarcoma, varix, cavernous hemangioma, racemose hemangioma, glomangioma, hemangiopericytoma, and acquired sessile hemangioma.

Prophylaxis

Prophylaxis is unclear for most vascular tumors. Eye protection can prevent trauma leading to development of pyogenic granulomas.

Therapy

Lymphangiomas are difficult to eradicate as both surgery and radiotherapy do not completely remove the mass.

Pyogenic granulomas can respond to topical corticosteroids, but some will still require surgical excision. Recurrent pyogenic granulomas can be treated with low-dose plaque radiotherapy (Shields et al. 2011a).

Capillary hemangiomas usually regress without treatment but can also be surgically resected. They regress in response to topical and systemic corticosteroids.

Varices are generally observed. There is a high risk of bleeding during surgical resection. If painful, cold compresses and aspirin can be used for pain relief.

Cavernous hemangiomas are treated definitely with surgical resection.

Hemangiopericytomas are managed by wide surgical resection with tumor-free margins.

Kaposi sarcoma is treated with cryotherapy and local or systemic chemotherapy. They have also been reported to be responsive to low-dose radiotherapy (Shields et al. 2011a).

Prognosis

All vascular conjunctival lesions are benign except for hemangiopericytomas and Kaposi sarcoma.

Epidemiology

These tumors are very uncommon, accounting for 4% of nonmelanocytic tumors of the conjunctiva (Shields et al. 2004).

Cross-References

- Conjunctiva
- Conjunctival Tumors
- Kaposi Sarcoma
- Pyogenic Granuloma

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VEGF Trap-Eye

► Antivascular Endothelial Growth Factor

Venereal Disease

► Syphilis: Overview

Venography, in Orbital Evaluation

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Definition

In medical applications of magnetic resonance imaging (MRI), a strong, uniform magnetic field is applied to water-containing tissue in order to align all protons into an excited state and subsequently measure their variable relaxation rates distinguish tissue types on imaging. These basic MR principles are extended with newer pulse sequence techniques and contrast-enhancement to image arterial and venous blood flow.

Purpose

The purpose of magnetic resonance venography is to detail venous blood flow to assess for anomalous vessels, aneurysms, stenosis, or abnormal connections between the arterial and venous circulations.

Principle

In their natural state, the atomic protons of any given tissue exhibit random movement. A polarizing magnetic field delivered by surface coils brings all of the protons into an excited state with uniform alignment to the external magnetic field. When the magnetic field is removed, the protons relax from this induced excited state back toward equilibrium at variable rates dependent on the tissue type they compose, and in doing so emit radio frequencies that are recorded by a receiving coil. There are two forms of relaxation which create the T1- and T2-weighted imaging. The differences in proton relaxation rates create the distinction between different tissues on images. A variety of magnetic pulse sequences can be applied to highlight different tissue types. However, vessels are not clearly imaged in conventional MR techniques because the fast flowing blood does not generate adequate signal from the proton relaxation.

The application of exogenous contrast in conventional catheter angiography can be used to visualize the vasculature and remains the gold standard for imaging of vascular lesions (e.g., aneurysms, carotid-cavernous fistulas, arteriovenous malformations). In catheter angiography, vessels are visualized with the aid of contrast along with adjacent tissues. In digital subtraction angiography, pre- and post-contrast images are subtracted to show exclusively the contrast-filled vessels. However, injection of contrast into the venous system carries inherent risks that, although small, can be avoided with newer imaging modalities. Computed tomography venography (CTV) and magnetic resonance venography (MRV) are among the newer imaging modalities available to ophthalmologists that allow for visualization of orbital vasculature while exposing patients to lower risks of morbidity (Black et al. 2012).

Magnetic resonance angiography (MRA) allows visualization of arterial blood flow with or without contrast through a variety of techniques, and detailed information can also be extracted about the venous system using specialized computer software. In MRV, the excited tissue is located directly inferior to the plane being imaged; thus, the signal is collected from blood as it drains

away from the excited plane (Haacke et al. 1999). A similar technique is used in MRA where the information can be further processed to easily create flow-velocity maps.

Indication

MRA and MRV can be helpful in any case where a vascular pathology needs to be further characterized or excluded. The primary ophthalmic indication for MRV is to exclude dural venous sinus thrombosis in the setting of elevated intracranial pressure and papilledema. The combination of MRI and MRV has been shown to increase the sensitivity of radiographic diagnosis of cerebral sinovenous thrombosis in children to 100% (Jackson et al. 2011). CTV can also be applied for this purpose in individuals who cannot tolerate prolonged imaging. Superior ophthalmic vein thrombosis is also well imaged with MRV and frequently appears on axial sections as the only structure coursing diagonally across the superior orbit.

In addition, orbital hemorrhages can be further characterized by MRA and MRV. In these cases, initial conventional CT or MRI may demonstrate a biconvex, well-defined, non-enhancing mass with increased density compared to the brain, which can be localized to the superior orbit in a subperiosteal hemorrhage, or can be more diffuse depending on the etiology. MR in particular can provide useful information about the age of the hemorrhage based on progressive decay of blood products. MRA and MRV are specifically helpful if there is concern for lesions with hemorrhagic potential (Black et al. 2012).

Contraindication

An individual patient may not be a good candidate for MRI if they have ferromagnetic implants in their body. The firmest contraindications include permanent pacemakers and pacing devices, nerve stimulators, cochlear implants, and certain aneurysm clips, but other types of implants may also be a relative contraindication (Levine et al. 2007). Moreover, in the event of orbital trauma, a CT scan is necessary to exclude the possibility of ferromagnetic foreign body prior to MRI.

Besides the technical constraints of MRI, the process of acquiring good quality, high-resolution MRIs requires a patient who is able to lie still for a prolonged period, often over 30 minutes. This may be impossible in medically unstable patients. The magnetic coil into which the person is inserted varies in size but is generally small, which can limit MRIs applicability in obese patients and require special planning for those with claustrophobia. Finally, MRI is considered safe in pregnant women, though the use of gadolinium-based (ferromagnetic) contrast is generally avoided (Webb and Thomsen 2013).

Advantage/Disadvantage

MRI is best applied for visualizing soft tissues and vasculature. Neurologic tissue is particularly well visualized, including the optic nerve and the brain. Innovations in surface coils, reduced signal-to-noise ratios, and fat-suppression on T1-weighted images have allowed steady improvements in orbital imaging. Pathology involving the bone – such as the cavernous sinus, orbital apex, and optic canal – produce relatively low signal on MRI and are generally better imaged with CT. Foreign bodies also typically produce poor signal on MRI, and given the risk of ferromagnetic material, are better examined with CT (Black et al. 2012).

Cross-References

- ▶ Arteriovenous Malformations (AVMs)
- ▶ Intraorbital Foreign Body (IOFB)
- ▶ Retrobulbar Hemorrhage

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Verisyse Iris-Supported Phakic Intraocular Lens

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Synonyms

Artisan iris-supported phakic intraocular lens; Iris-fixated phakic intraocular lens

Definition

A phakic IOL that is enclavated on the iris with specially designed "iris-claw" haptics.

Epidemiology

Before introduction of the latest phakic IOL model (AcrySof), the iris-supported phakic IOL models (Artisan/Verisyse and Artiflex/Veriflex) were the most frequently implanted anterior chamber phakic IOLs (Kohnen and Koch 2006).

History

The iris-claw phakic IOL was initially used in aphakic eyes after intracapsular cataract extraction. Starting in 1953, the first-generation models such as the Binkhorst lens and the Medallion lens were associated with cystoid macular edema, corneal decompensation, lens dislocation, uveitis, and glaucoma (Hardthen et al. 2003). In 1978, J. Worst designed the iris-claw or "lobster-claw" IOL, a coplanar one-piece PMMA IOL, which was enclavated in a fold of mid-peripheral iris stroma, a relatively immobile portion of the iris. Many surgeons have used the iris-claw lens after intracapsular cataract extraction or as secondary implantation in aphakia. In 1986, Fechner implanted the first sighted myopic phakic eye (Fechner and Alpor 1986). Follow-up of Fechner-Worst lens implantation showed good predictability but a progressive corneal endothelial cell loss. The currently available iris-claw model is basically the original IOL with few changes and with less likelihood of endothelial cell loss.

Clinical Features

The Verisyse/Artisan phakic IOL is made of a single-piece, non-foldable, ultraviolet light-absorbing PMMA material. It is available for the correction of myopia, hyperopia, and astigmatism, as well as for aphakia. The optic vaults approximately 0.87-mm anterior to the iris, allowing for an important clearance from both the anterior lens capsule and the corneal endothelium. The distance from the optic edge to the endothelium ranges from 1.5 to 2 mm depending on dioptric power, anterior chamber anatomy, and diameter of the optic. There are two models available to correct myopia: model 206 has a 5.0-mm optic with power ranging from −3 to −23.5 diopters (D) in 0.5-D increments and model 204 has a larger 6.0-mm optic and is

consequently limited to a smaller range of powers because of its greater proximity to the endothelium in the periphery of the IOL, −3 to −15.5 D in 0.5-D increments. For the correction of hyperopia, model 203 incorporates a 5-mm optic, and it is available in dioptric powers ranging from +1 to + 12 D in 0.5-D increments. Myopic lenses require more clearance than hyperopic due to thicker peripheral edges. The thickest part of the hyperopic IOL on the other hand is central, where the anterior chamber depth is greater. The toric model has a 5-mm optical zone and is available in powers ranging from +12 D to −23.5 D in 0.5-D increments, with additional cylinder from +1.0 D to +7.0 D, also in 0.5-D increments, and oriented either at 0° or at 90°. It has a fixed overall length of 8.5 mm (7.5 mm for pediatric implantations or small eyes), which is a great advantage to the surgeon who does not wish to deal with sizing measurements.

Tests

Anterior chamber depth for Artisan/Verisyse phakic IOL implantation must be at least 2.7 mm. Other inclusion criteria for phakic IOL implantation must be considered (see also "► phakic intraocular lens").

Differential Diagnosis

Other currently available types of phakic IOLs are anterior chamber angle (AcrySof) or posterior chamber (phakic refractive lens and implantable collamer lens) phakic IOLs.

Etiology

On the European market, this phakic IOL is distributed as ArtisanÒ (Ophtec B. V., Groningen, The Netherlands) and in the USA as VerisyseÒ (Abbott Laboratories, Abbott Park, Illinois, USA). The foldable model of the iris-claw lens is the Artiflex/Veriflex phakic IOL, which has a hydrophobic polysiloxane foldable design with a 6.0-mm optic.

Treatment

For Artisan/Verisyse implantation, retrobulbar or peribulbar anesthesia is recommended. A - two-plane, 5.2- or 6.2-mm posterior corneal incision is centered at 12 o'clock, and two vertical paracenteses directed to the enclavation area are performed at 2 and 10 o'clock. Alternatively, scleral incision may be used. Pupil should be constricted to protect the crystalline lens from contact with the phakic lens or instruments. After the anterior chamber is filled with viscoelastic material, the lens is introduced and rotated 90° into horizontal position. The lens is fixed with an enclavation needle that has a bent shaft and a bent tip that pushes the iris into both claws. Peripheral iridectomy should be performed to prevent pupillary block situation. Alternatively, Nd/YAG laser can be used preoperatively to create one or two small iridotomies 90° apart. The corneal wound is then sutured with five interrupted 10-0 nylon stitches, the scleral incision with one running suture (Güell et al. 2010).

Cross-References

► Artisan Lens
► Foldable Intraocular Lens
► Intraocular Lens
► Phakic Intraocular Lens

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Vernal Conjunctivitis

▶ Palpebral Vernal Conjunctivitis/ Keratoconjunctivitis

Vernal Conjunctivitis/ Keratoconjunctivitis

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Synonyms

Spring catarrh; VKC

Definition

Vernal conjunctivitis is a disease characterized by bilateral, recurrent inflammation of the conjunctiva that often has a seasonal incidence (Bonini et al. 2004). It is a member of a group of diseases that are all considered allergic conjunctivitis such as seasonal rhinoconjunctivitis and atopic keratoconjunctivitis (Bonini et al. 2004). It is more common in patients with an atopic background (Kumar 2009).

Etiology

The exact etiology of vernal conjunctivitis is unknown, but it is thought that the pathogenesis is multifactorial with immune, nervous, and endocrine systems all playing a role (Bonini et al. 2004). It is thought that IgE-mediated hypersensitivity and T helper cell type 2 (Th2)-mediated responses play major roles in pathogenesis (Kumar 2009). Patients often have a family history of other atopic diseases (Bonini et al. 2004).

Clinical Presentation

The most typical presentation of a patient with vernal conjunctivitis would include bilateral ocular itching and filamentous, sticky discharge (Gerstenblith et al. 2012). However, sometimes patients can initially present unilaterally. There is also often bilateral hyperemia, chemosis, photophobia, and lacrimation (Bonini et al. 2004).

The disease can present as a palpebral or limbal disease, but a range of mixed appearances also exists (De Smedt et al. 2013). The disease is often characterized by the appearance of giant papillae that create a cobblestone appearance at the upper tarsal conjunctiva or at the limbus (Gerstenblith et al. 2012). Aggregates of epithelial cells and eosinophils at the limbus known as Trantas dots are also often seen in the disease (Bonini et al. 2004). Subconjunctival fibrosis, symblepharon, and conjunctival keratinization can also occur in the disease (Bonini et al. 2004). The cornea can be damaged with a superficial keratopathy or the presence of corneal shield ulcers (Bonini et al. 2004).

Diagnosis

The diagnosis of vernal conjunctivitis is often made clinically based upon the epidemiology and clinical findings of the patient (Bonini et al. 2004). Currently, total and specific IgE determination and other skin tests are not useful as laboratory tests, because many patients with the disease will test negative on these tests (Bonini et al. 2004). Eosinophils found in conjunctival scrapings of patients can help support the diagnosis of vernal conjunctivitis (De Smedt et al. 2013).

Differential Diagnosis

The differential diagnosis includes:

- Atopic keratoconjunctivitis
- Seasonal allergic conjunctivitis
- Giant papillary conjunctivitis
- Bacterial conjunctivitis

Prophylaxis

Use a mast cell stabilizer and/or antihistamine 2–3 weeks prior to allergy season (Gerstenblith et al. 2012). Also, patients should avoid common

triggers such as sun, wind, and salt water and avoid contact with common allergens like plants (Kumar 2009).

Therapy

Treatment of vernal conjunctivitis is similar to that of other allergic conjunctivitis. Topical antihistamines and mast cell stabilizers are usually the first-line treatment (Bonini et al. 2004). Nonsteroidal anti-inflammatory drug topical agents have been shown to have a beneficial effect on the course of the disease (De Smedt et al. 2013). Topical corticosteroids are used in moderate to severe forms of the disease, but their use has to be carefully monitored due to potential long-term side effects such as glaucoma (De Smedt et al. 2013). Cyclosporin A can be used for severe disease when patients also have a shield ulcer (Gerstenblith et al. 2012). Surgical excision is sometimes utilized if the giant papillae cause corneal lesions (Kumar 2009).

Prognosis

Patients with vernal conjunctivitis often have spontaneous resolution of their disease after puberty (Bonini et al. 2004). However, a small percentage of patients can have permanent visual damage if they develop cataracts, glaucoma, or corneal ulcers as part of their disease (Bonini et al. 2004). Furthermore, if patients do have a chronic disease course, it can increase their risk for developing keratoconus (De Smedt et al. 2013). Negative prognostic signs include having larger papillae (Bonini et al. 2004).

Epidemiology

Vernal conjunctivitis mainly affects young patients in their first or second decade (De Smedt et al. 2013). It is more common in boys than girls (Bonini et al. 2004). The disease is rare in temperate regions; however, in areas such as Africa, Latin America, and Asia, it has a higher prevalence with some parts of Africa having a 4–5% population prevalence (De Smedt et al. 2013). Vernal conjunctivitis also has a seasonal variation with flare-ups often occurring during spring/summer months (De Smedt et al. 2013). However, the disease can be present year-round, and initial seasonal disease can become perennial (Bonini et al. 2004).

Cross-References

- ▶ Allergic Conjunctivitis
- ▶ Palpebral Vernal Conjunctivitis/Keratoconjunctivitis

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Vernier Acuity

▶ Hyperacuity (Vernier Acuity)

Verruca

▶ Verruca Vulgaris

Verruca Vulgaris

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Synonyms

Common wart; Verruca; Viral papilloma

Definition

Verruca vulgaris is a benign epithelial hyperplastic skin lesion thought to be caused by a viral infection.

Etiology

The human papilloma virus (HPV), is correlated to a DNA virus, verruca vulgaris. These lesions are spread by direct contact or autoinoculation and may occur anywhere on the skin, occasionally on the eyelid (Albert and Jakobiec 2008).

Clinical Presentation

Lesions appear elevated, multilobulated, grape-like, and with an irregular, hyperkeratotic, papillomatous surface. Lesions along the eyelid margin may induce a mild papillary conjunctivitis due to shedding of virus particles into the tear film. Patients also may develop a superficial punctuate keratitis and have pannus formation (Albert and Jakobiec 2008).

Diagnostics

Based on the typical appearance of clinical findings and may be confirmed by biopsy.

Differential Diagnosis

Differential diagnosis includes ▶ actinic keratosis, ▶ molluscum contagiosum, ▶ seborrheic keratosis, and ▶ squamous cell carcinoma.

Prophylaxis

Avoid contact.

Therapy

Observation is recommended if no ocular complications occur. Treatment, if necessary, includes topical agents, intralesional injections, systemic agents, cryotherapy, laser, electrodessication, and surgical excision (Nesi et al. 1998).

Prognosis

Recurrences are common. Spontaneous regression is also common. Rarely, squamous cell carcinoma may develop in verruca vulgaris, usually in immunocompromised patients (Albert and Jakobiec 2008).

Epidemiology

A peak incidence in late childhood and early adulthood.

Cross-References

- ▶ Actinic Keratosis
- ▶ Molluscum Contagiosum
- ▶ Papillomas, Eyelid
- ▶ Squamous Cell Carcinoma of Eyelid

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Verrucous Lesion

▶ Human Papilloma Viruses, Ocular Infection

Vertebrobasilar Atherothrombotic Disease (VBATD)

▶ Diplopia in Vertebrobasilar System Disease

Vertebrobasilar Insufficiency (VBI)

▶ Diplopia in Vertebrobasilar System Disease

Vertex Keratopathy

▶ Chloroquine Toxicity, Cornea Verticillata

Vertical Eyelid Splitting, for Anterior Orbitotomy

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Definition

An anterior orbitotomy performed by creating a vertical incision through the eyelid margin to allow broader exposure to the anterio-medial orbit.

Indications

To obtain wider access to the superiormedial intraconal space for biopsy, lesion excision, or optic nerve fenestration.

Contraindication

Lesion deeper in the orbit or not able to be accessed via anterior orbitotomy. Any medical contraindication to surgery.

Techniques and Principles

This procedure is generally performed in the operating room under sedation or general anesthesia. An incision is marked vertically at the junction of the medial one-third and lateral two-thirds of the upper eyelid. The incision is made full thickness through the eyelid and requires proper realignment of the tarsal plate and anterior lamella in multiple layers at the close of the procedure (Nerad 2001; Levine 2003).

Outcome

Allows for wider exposure biopsy, lesion removal, foreign body removal, and orbital decompression as necessary.

Complications

Risks of the vertical eyelid splitting technique include risks associated with anesthesia, bleeding, pain, infection, scarring, swelling, loss of vision, damage to adjacent structures, diplopia, ptosis, eyelid retraction, and need for additional procedures (Nerad 2001; Levine 2003).

Cross-References

▶ Anterior Orbitotomy
▶ Optic Nerve (Cranial Nerve II)
▶ Orbital Cellulitis

References

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Vertical Gaze Palsy

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Synonyms

Upgaze palsy

Definition

Vertical gaze palsy (VGP) is a conjugate gaze palsy that results in the inability to move both eyes in a single vertical direction (upgaze or downgaze or both). It usually occurs bilaterally; however, it is occasionally seen unilaterally (Rubin 2014).

Epidemiology

VGP can affect any age, either gender, and any racial group depending on underlying etiology.

History

One of the first clinical descriptions of VGP was published in 1964. In this case report, vertical gaze palsy was reported as a clinical manifestation of progressive supranuclear palsy (PSP) (Steele et al. 1964).

Clinical Features

Patients with VGP often track objects moving their head instead of the eyes, especially during a routine eye exam (Rubin 2014). The doll's head maneuver can be used to activate the vestibular ocular reflex to move the eyes vertically (up- and downgaze) if the lesion is supranuclear and the infranuclear pathways are intact.

Tests

Limited up and down eye movements during a routine eye exam can be used as an initial diagnosis. In addition, neuroimaging should be conducted to visualize the suspected midbrain lesion(s) or supranuclear lesion(s). Myasthenia gravis and thyroid ophthalmopathy can mimic VGP (Rubin 2014).

Differential Diagnosis

- Dilated pupil
- Vertical nystagmus during upward gaze

Etiology

Lesions in the midbrain (stroke or tumor) are causes of bilateral, symmetric VGP. Common locations of lesions include interstitial nucleus of Cajal and the rostral interstitial nucleus of the medial longitudinal fasciculus (Rubin 2014). The differential diagnosis for VGP includes stroke, tumor, demyelination, degeneration

(e.g., progressive supranuclear palsy), hydrocephalus, shunt failure, and other lesions of the thalamomesencephalic junction or dorsal midbrain (Benjamin 1999).

Treatment

Treatment should be directed to the underlying etiology (Rubin 2014).

Cross-References

- ▶ Interstitial Keratitis
- ▶ Longitudinal Chromatic Aberration
- ▶ Parinaud (Dorsal Midbrain) Syndrome
- ▶ Progressive Supranuclear Palsy

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Vetalog

- ▶ Intravitreal Triamcinolone

VHL

- ▶ VHL Syndrome

VHL Syndrome

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Synonyms

Angiomatosis retinae; Cerebelloretinal hemangioblastomatosis; Familial cerebello-retinal angiomatosis; Hippel disease; Hippel–Lindau syndrome; HLS; Lindau disease or retinocerebellar angiomatosis; VHL; von Hippel–Lindau disease

Definition

von Hippel–Lindau disease (VHL) is a rare autosomal dominant condition that causes benign and malignant tumors and cysts in the central nervous system (CNS) as well as visceral organs. VHL results from a mutation in the VHL tumor suppressor gene on chromosome 3p25.3. One of the most common findings in VHL patients are

hemangioblastomas of the retina or optic nerve head. A hemangioblastoma is any case of angiomatosis, a proliferation of vascular endothelium, within the central nervous system. Retinal capillary hemangioblastomas are found in up to 70% of VHL patients by 60 years of age (Kreusel et al. 2006). This extremely high prevalence results in a high risk of vision loss starting at a young age and requires regular lifelong ophthalmic screening. Similarly, 60–84% of VHL patients develop hemangioblastomas of the brain or spinal cord. Other common tumors associated with VHL disease are pheochromocytoma, renal cell carcinoma, renal cysts, pancreatic cystadenoma, and pancreatic neuroendocrine tumors (Shuin et al. 2006).

Etiology

VHL is an autosomal dominant disorder caused by a mutation and loss of function of the VHL tumor suppressor gene located on chromosome 3p25–26. Over 1,500 mutations of this gene have been identified in patients with VHL. Approximately 20% of mutations are de novo, with the other 80% being inherited. Tumors form only in cells which have mutations in both copies of the VHL tumor suppressor gene (two-hit hypothesis). The loss of function of the VHL protein results in the cell's inability to break down hypoxia-inducible factors (HIFs) and other proteins. HIFs are the major transcription factors under hypoxic conditions and are usually degraded (ubiquitinated) under normoxic conditions. High levels of HIFs lead to the transcription of large amounts of vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and transforming growth factor alpha (TGF-α). These cytokines lead to the accelerated and abnormal proliferation of microvasculature known as angiomas. Within the CNS, focal collections of these angiomas are called hemangioblastomas (Dollfus et al. 2002; Shuin et al. 2006).

Clinical Presentation

The mean age at initial diagnosis of VHL disease is approximately 29 years. Retinal hemangioblastoma is the ophthalmological hallmark of VHL disease and is often the clinical sign that first leads to diagnosis. Retinal hemangioblastomas can develop from a very early age until around 30 years of life. After this age, the frequency gradually decreases. When caught early, the first clinical presentation is typically unilateral and often without symptoms. In later stages, about half of VHL patients with retinal manifestations develop bilateral disease. Juxtapapillary lesions can cause pseudopapilledema. Tractional retinal detachment is also a significant risk if hemangioblastomas are left untreated and may be the cause of presenting symptoms. Retinal hemangioblastomas can be detected by ophthalmoscopy, fluorescein angiography, or wide-field retinal imaging. Fluorescein angiography typically shows early leakage and hyperfluorescence. Macular edema caused by these growths can be identified on optical coherence tomography (OCT). Patients identified as high risk by genetic screening or family history should be seen by an ophthalmologist annually starting at preschool age (Shuin et al. 2006; Wong et al. 2007).

Hemangioblastomas may also present in other regions of the CNS. Excluding the retina, approximately 50% of VHL hemangioblastomas occur in the spinal cord, 40% in the cerebellum, and 10% in the brainstem. In these locations, symptoms can present as the result of compression of neural structures, bleeding, or paraneoplastic complications. In patients with VHL, routine screening of the neuroaxis via MRI is recommended starting after 10 years of age.

Diagnostics

Retinal hemangioblastomas can be diagnosed by ophthalmoscopy, fluorescein angiography, or wide-field retinal imaging. Fluorescein angiography

typically shows early leakage and hyperfluorescence. Macular edema caused by these growths can be identified on optical coherence tomography (OCT). For hemangioblastomas of the brain or spinal cord, gadolinium-enhanced magnetic resonance imaging (MRI) offers the best resolution. A family history of VHL disease should be sufficient for diagnosis; however, screening by southern blot and genetic sequencing may be necessary for many patients (Kreusel et al. 2006).

Differential Diagnosis

Coats disease, racemose hemangioma, retinal cavernous hemangioma, and retinal macroaneurysm can present similarly to retinal hemangioblastomas. However, a detailed family history and/or genetic screening are all that are needed to make an accurate diagnosis of retinal hemangioblastomas associated with VHL.

Prophylaxis

No method of prophylaxis has been identified.

Therapy

Multiple treatment modalities have been proposed for the management of retinal hemangioblastomas secondary to VHL disease. Depending on the location of the lesion being targeted and its associated findings, laser photocoagulation, cryotherapy, photodynamic therapy, surgical excision, enucleation, or very often just observation may be indicated. Laser photocoagulation has proven to be the most effective at controlling peripheral lesions. Anti-VEGF therapy has been proposed as an adjunct therapy to VHL management; however, small studies have suggested limited efficacy on the tumor itself, while reducing associated macular edema (Shuin et al. 2006).

Prognosis

The prognosis of VHL patients depends on the location and complications of the tumors. In one longitudinal study, visual acuity worse than 20/1,000 was reported in 20% of effected eyes by age 20 and 50% of effected eyes by age 30. Another study found that visual morbidity increases with the hemangioblastoma count. A large genetic study correlating genotype and phenotypes found that VHL patients with complete deletions of the VHL protein have the lowest prevalence of ocular disease and the most favorable visual outcomes (Shuin et al. 2006).

Epidemiology

VHL has been estimated to affect 1 in 36,000 births. In the USA and Europe, 70% of VHL patients develop retinal hemangioblastomas, while Japanese VHL patients have a significantly lower risk (<40%). Similarly, 60–84% of VHL patients develop hemangioblastomas elsewhere in the CNS. Approximately 50% of these occur in the spinal cord, 40% in the cerebellum, and 10% in the brainstem (Shuin et al. 2006).

Cross-References

- ▶ Hemangioblastomas, with Retinal Angiomatosis (von Hippel Lindau Disease)
- ▶ Retinae (Retinal Angiomatosis, von Hippel Syndrome/Disease)

References

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Videokeratography

▶ Computerized Corneal Topography

Viral Keratitis with Ulceration

▶ Ulcerative Keratitis Disease

Viral Papilloma

▶ Verruca Vulgaris

Viscoelastic Agents

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Synonyms

Ophthalmic viscosurgical device (OVD)

Definition

Clear, soft substances with a texture ranging from honey to jam which have become essential to modern anterior segment surgery, consisting of any or a combination of the following substances: hydroxypropyl methylcellulose, sodium hyaluronate, and chondroitin sulfate. They aid surgery because they create space, protect the corneal endothelium and tamponnade structures (for example, they can be used to hold vitreous posterior). These agents flow easily when higher forces are applied to them but retain their original shape when a lower force is applied.

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Viscoelastic Substances

▶ Ophthalmic Viscosurgical Devices

Visual Agnosia

▶ Agnosia, Object

Visual Conversion

▶ Nonorganic Visual Loss

Visual Form Agnosia

▶ Agnosia, Object

Visual Migraine

▶ Retinal/Ocular Migraine

Visual Perseveration

▶ Palinopsia

Visual Release Hallucinations

▶ Charles Bonnet Syndrome: Overview

Visual Release Phenomena

▶ Charles Bonnet Syndrome: Overview

Visuomotor Ataxia

▶ Ataxia, Optic

Vitamin A

▶ Beta Carotene, Use and Dosage of

Vitamin A Deficiency

▶ Xerophthalmia

Vitelliform Macular Dystrophy

▶ Best Disease

Vitelliform Macular Dystrophy Type 2

▶ Best Disease

Vitiliginous Chorioretinitis (No Longer Used)

▶ Birdshot Retinochoroidopathy (Vitiliginous Chorioretinitis)

Vitrectomy

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Synonyms

Anterior vitrectomy; Core vitrectomy; Pars plana vitrectomy

Definition

Surgical procedure to remove the vitreous or part thereof from the vitreous cave.

Epidemiology

Formerly related to a large variety of serious complications, vitrectomy – especially small gauge pars plana vitrectomy – has become a widely used technique for a large number of pathologies. To date approximately 200,000 vitrectomies are performed in the USA per year (Fabian and Moisseiev 2010; Recchia et al. 2010).

History

Up to the late 1960s, vitreous dissection was a general problem. Formerly, a vitrectomy was performed as so-called swap-vitrectomy. Here, the vitreous was soaked-up by the aid of a swap and cut thereafter using scissors. This was only possible during open-globe conditions.

Established as a single port 19 gauge procedure by Robert Machemer in 1969, it was then possible to extract vitreous in a closed system providing constant intraocular pressure. This procedure was

first used for vitreous hemorrhage. However, further technical improvement established vitrectomy as a widely used technique for a large variety of pathologies.

Clinical Features

Excision of the vitreous is usually performed using a specially designed cutter. This cutting tool usually consists of a tube with an oscillating knife. By applying suction, the vitreous is sucked into the tube and cut by the oscillating knife. Sizes of this so-called cutter may differ from 20 to 27 gauge.

The properties of a cutter are highly dependent suction, cutting rate, infusion, size, and design of the notch of the cutter.

Nowadays, there are different forms of vitrectomy. While in anterior vitrectomy, part of the anterior vitreous is removed mainly transpupillary, the access during pars plana vitrectomy is transcleral through pars plana. Core vitrectomy is a technique that refers to excision of only the central vitreous.

Tests

Efficacy of this surgical procedure has been demonstrated for a large number of pathologies.

Etiology

See history.

Treatment

Vitrectomy is performed in a large variety of pathologies ranging from posterior capsule rupture during cataract surgery to retinal detachment and macular surgery.

Cross-References

► Cataract Surgery
► Macular Holes
► Pars Plana Vitrectomy
► Retinal Detachment

References

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Vitreolysis, Enzymatic

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Definition

Process of manipulating the central vitreous collagen or cortical vitreous at the retinal interface with chemicals and enzymes rather than with mechanical instruments. Historically, enzymatic vitreolysis has been accomplished with chondroitinase, hyaluronidase, dispase, or plasmin.

Indication

The potential applications for enzymatic vitreolysis are numerous and include any condition that involves an abnormal vitreoretinal interface, with or without retinal traction. At present, no formal list of indications is available since enzymatic vitreolysis remains predominantly investigational. Nonetheless, enzymatic vitreolysis may be advantageous over mechanical vitrectomy whenever mechanical dissection is arduous or poses a risk to vital intraocular structures. Conditions that have been studied with enzymatic vitreolysis include advanced retinopathy of prematurity (stage 4 and stage 5), pediatric macular holes, diabetic macular edema,

and x-linked retinoschisis (Chen et al. 2008; Trese 2002; Wu et al. 2007).

Contraindication

Absolute contraindication for enzymatic vitreolysis includes a history of an allergic reaction to a specific enzyme. Additional contraindications will likely be forthcoming as future research indentifies which patients do not benefit from enzymatic vitreolysis.

Use and Dosage

Enzymatic vitreolysis is typically administered via an intravitreal injection. For eyes scheduled to undergo mechanical vitrectomy, the intravitreal injection of the enzyme is performed shortly before surgery.

Plasmin is usually given at doses between 0.4 IU and 2.0 IU, although amounts as large as 3 IU appear to be well tolerated. At these doses, intravitreal plasmin liquefies the vitreous and provides for easier peeling of cortical vitreous in conditions such as macular hole, diabetic retinopathy, x-linked retinoschisis, and retinopathy of prematurity. Enzymatic activity peaks within 15–30 min of the intravitreal injection, remains elevated for 1–2 h, and decreases to an undetectable level after several hours. Presently, intravitreal plasmin for intravitreal use is not commercially available and remains costly and time-consuming to obtain. Recombinant microplasminogen may soon be a reasonable substitute for autologous plasmin (Chen et al. 2008).

Hyaluronidase for intravitreal use also remains investigational. It recently underwent phase III testing as an adjunct for clearing vitreous hemorrhage, but failed to meet its efficacy end point in this study and did not receive FDA approval. It should be recognized that intravitreal hyaluronidase is distinctly different from the subcutaneous hyaluronidase, which is currently available as a spreading agent for anesthesia under the commercial name of Vitrase (ISTA Pharmaceuticals; Irvine, California).

Chondroitinase likewise remains investigational. It has been studied in phase I human trials, but no specific data is yet available.

Adverse Reactions

Since enzymatic vitreolysis is administered via an intravitreal injection, adverse reactions are similar to those for all intravitreal injection, including allergic reaction, cataract formation, endophthalmitis, vitreous hemorrhage, retinal tear, and retinal detachment. In addition, sterile inflammation with hypopyon has been described following hyaluronidase.

Interactions

No interaction has yet been described between these vitreolytic enzymes and any systemic medication. This may be due to the short duration of activity for these intraocular enzymes and the confinement of biological activity to the vitreous cavity following intravitreal injection.

Cross-References

- ▶ Pars Plana Vitrectomy
- ▶ Vitrectomy
- ▶ Vitreous Humor

References

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Vitreon

- ▶ Perfluorocarbon

Vitreous Base Avulsion, "Bucket-Handle Sign"

▶ Anterior Vitreous Detachment, Contusion Injury Causing

Vitreous Base Detachment

▶ Anterior Vitreous Detachment, Contusion Injury Causing

Vitreous Humor

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Synonyms

Hyaloid

Definition

The vitreous is a transparent gel-like tissue that fills the posterior portion of the eye, extending from the posterior lens capsule to the internal limiting membrane of the retina. It occupies about four fifth of the eye, has a volume of about 4 ml, and weighs about 4 g.

Structure

The vitreous is a matrix of collagen filaments, hyaluronan acid, water, and rare cells called hyalocytes. Biochemically, the vitreous is about 99% water, 1.0% inorganic salts and organic lipids, and 0.1% soluble and insoluble proteins and hyaluronan acid. Collagen filaments form a framework to which hyaluronan acid binds. These hyaluronan acid molecules attract water, and together they act as spacers between adjacent collagen fibers. With age, the hyaluronan acid dissociates from the collagen filament framework. This results in more fibrous collagen filament aggregations and liquefaction of the vitreous.

Although the vitreous is continuous with all tissues it touches, it is only firmly attached in specific locations. Usual areas of attachment include the vitreous base, the margin of the optic nerve, the foveal and parafoveal areas of the macula, along major retinal vessels, and retinal tufts. The vitreous may also be more adherent to areas of lattice degeneration, areas of retinal degeneration remodeling, and some post-inflammatory lesions.

Function

The vitreous is a clear media that fills the eye and allows for light to pass through it to the retina. The vitreous also helps to modulate ocular development. During embryogenesis, the primary vitreous develops between the lens and optic cup and contains the hyaloid artery. The secondary avascular vitreous forms around the primary vitreous, creating the walls of the canal of Cloquet. A yet unknown stimulus signals for regression of the hyaloid artery around the third month post-conception, leading to the regression of the primary vitreous. The vitreous becomes more transparent, allowing for less light scatter as it enters the eye.

Clinical Relevance

Failure of regression of the primary vitreous can lead to several congenital anomalies, some that can dramatically affect on vision. These include persistent hyperplastic primary vitreous (PHPV) in which the primary vitreous and fetal vasculature fails to regress, a persistent opacity on the posterior lens capsule called a Mittendorf's dot, and a persistent vascular loop that extends into the vitreous from the optic nerve head called a Bergmeister's papilla.

A very common age-related change in the vitreous is a posterior vitreous detachment (PVD).

Liquefaction of the vitreous and collapse of the extracellular matrix of the vitreous lead to separation of the posterior vitreous base from the internal limiting membrane of the retina. Vitreous detachments can be localized, partial, or complete to the vitreous base. PVDs are more likely to occur as the eye ages. Eyes that are myopic or that have undergone cataract surgery have a greater occurrence of PVDs. Vitreous traction at areas of adhesion to the retina during a PVD can lead to retinal tears and retinal detachment.

Diseases associated with collagen disorders can have anomalous PVDs where liquefaction of the vitreous occurs without release of vitreoretinal adhesions. The resulting tractional forces can lead to large retinal tears and retinal detachments. Systemic diseases with collagen metabolism disorders where anomalous PVDs can occur include Marfan's, Sticklers, and Ehlers-Danlos syndromes.

Vitreoretinal adhesions to the retina can lead to the formation of macular edema as seen in vitreomacular traction syndrome and in patients with diabetes. With trauma, tractional forces by the vitreous on the retina can also result in macular hole formation retinal hemorrhages, or peripheral retinal tears and detachment. When the vitreous adheres to retinal blood vessels, as seen with neovascularization in proliferative diabetic retinopathy, vitreous hemorrhages can result.

There are many types of vitreous opacities. As the vitreous matrix collapses, bands of collagen form strands that can be seen as floaters. Inflammatory vitreous cells and vitreous cell collections called snowballs are common with pars planitis and posterior uveitis. Other opacities include calcium crystals called asteroid hyalosis, red blood cells, pigmentary cells, and tumor cells. Cysts may also form in the vitreous.

Cross-References

- ▶ Asteroid Hyalosis
- ▶ Bergmeister's Papilla
- ▶ Ehlers-Danlos Syndrome, Angioid Streaks in
- ▶ Marfan Syndrome
- ▶ Persistent Hyperplastic Primary Vitreous
- ▶ Posterior Vitreous Detachment
- ▶ Stickler Syndrome (Hereditary Progressive Arthro-Ophthalmopathy)

Further Reading

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Vitreous Lamina (*Lamina Vitrea*)

- ▶ Bruch's Membrane

Vitreous Substitute

- ▶ Perfluorocarbon

Vivid Visual Hallucinations

- ▶ Charles Bonnet Syndrome: Overview

VKC

- ▶ Vernal Conjunctivitis/Keratoconjunctivitis

Vogt Lines, Keratoconus

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Synonyms

Vogt striae

Definition

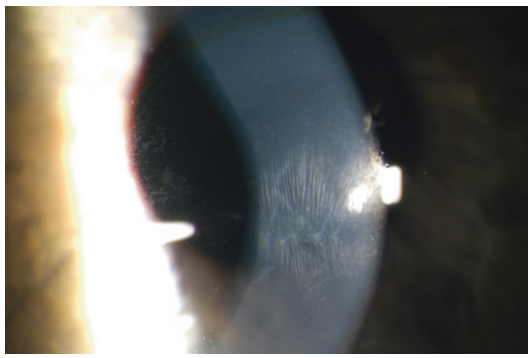
Fine vertical striations in Descemet's membrane and the posterior stroma that may be seen in the keratoconic cornea (Fig. 1).

Etiology

One of the classic clinical signs used to diagnose keratoconus that may be detected on slit-lamp examination of the cornea (other signs on slit-lamp examination include stromal thinning, corneal protrusion, Fleischer or iron ring, anterior stromal scars, and enlarged corneal nerves). Vogt lines or striae are fine lines running in a largely vertical direction in the deep stroma and Descemet's membrane that parallel the steepest axis of the cone and radiate from the center of the cone. Confocal microscopy suggests that these striae represent stress-related changes in the collagen lamellae (Hollingsworth and Efron 2005). These lines disappear transiently when intraocular pressure is raised by applying external pressure on the globe or by wearing a gas permeable rigid contact lens (Barbara 2012).

Occurrence

Of 1,209 patients with keratoconus enrolled at 16 sites across the United States between 1995 and 1996 in the Collaborative Longitudinal Evaluation of Keratoconus study, Vogt's striae were present unilaterally in 35% of the population and bilaterally in 30% of the population at baseline (Wagner et al. 2007).



Vogt Lines, Keratoconus, Fig. 1 Slit-lamp examination demonstrates fine vertical lines in a keratoconic eye consistent with Vogt lines

Cross-References

- ▶ Corneal Ectasia
- ▶ Keratoconus

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Vogt Striae

▶ Vogt Lines, Keratoconus

Vogt's Crocodile Shagreen Dystrophy

▶ Shagreen, Crocodile

Volonimat

▶ Intravitreal Triamcinolone

Voluntary Gaze Paresis

▶ Ocular Motor Apraxia

von Hippel–Lindau Disease

▶ VHL Syndrome

Von Hippel-Lindau Disease, VHL

▶ Hemangioblastomas, with Retinal Angiomatosis (von Hippel Lindau Disease)

Von Hippel–Lindau Disease, VHL

▶ Retinae (Retinal Angiomatosis, von Hippel Syndrome/Disease)

Vortex (Hurricane) Keratopathy

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Synonyms

Cornea verticillata

Definition

Vortex keratopathy (VK) is an ocular condition characterized by whorl-like grayish, whitish, or golden-brown corneal epithelial deposits (Hollander and Aldave 2004). When the whorl pattern is highlighted with fluorescein, it is known as hurricane keratopathy (Dua and Gomes 2000).

Etiology

Proliferating corneal epithelial cells migrate from the limbus toward the corneal center on a regular basis to replace terminally differentiated cells that are shed from the superficial layer. The cells follow a curvilinear track, leading to a vortex or whorl pattern in the cornea. Normally this path is not visible, but intracellular collection of substances like pigment, iron, drug metabolites, glycogen, and sphingolipid can highlight the vortex or whorl pattern leading to VK. This pattern on the corneal surface can also be seen when epithelial cell turnover is increased, e.g., in contact lens wearers and corneal graft recipients. In such situations, pattern is highlighted by fluorescein and is called "hurricane keratopathy." The proposed explanation for this phenomenon of being highlighted by fluorescein is that rapidly proliferating cells have poor intercellular adhesions allowing fluorescein to collect around and outline the cells (Dua and Gomes 2000).

A large number of medications are associated with VK including aminoquinolines (e.g., chloroquine, hydroxychloroquine), amiodarone, atovaquone, clofazimine, subconjunctival gentamicin, gold, ibuprofen, indomethacin, mepacrine, monobenzone, naproxen, perhexiline maleate, phenothiazines, suramin, tamoxifen, and tilorone hydrochloride (Hollander and Aldave 2004).

VK is also seen in Fabry's disease, an X-linked disorder leading to accumulation of glycosphingolipids within lysosomes due to deficiency of enzyme alpha galactosidase A. The VK pattern seen in Fabry's disease was first described by Francois in 1968 and noted to cause intralysosomal deposits, and the pattern was shown to be identical to the one associated with medication use (D'amico and Kenyon 1981; Dua et al. 1996; Hollander and Aldave 2004).

It is thought that the diverse medications and their metabolites enter lysosomes and bind with cellular lipids. The complexes, thus formed, tend to accumulate within the lysosomes. The whorl-like patterns are due to the centripetal migration of the limbal epithelial cells carrying these molecules (Hollander and Aldave 2004).

Occurrence

VK is seen in 69–100% of patients on 200–1,400 mg of amiodarone, is usually bilateral and symmetrical, and resolves within

3–20 months of cessation of drug. It is usually asymptomatic and its development is not an indication for discontinuing amiodarone treatment. Twenty-eight to 95% of patients on chloroquine and 1–28% on hydroxychloroquine develop verticillata (Hollander and Aldave 2004) When medications are stopped, VK fades away and resolves.

The whorl pattern in hurricane keratopathy persists for as long as there is stimulus for increased cell turnover. Once that stimulus is gone, the whorl pattern in the cornea resolves spontaneously (Dua and Gomes 2000).

VK is the most common ocular manifestation of Fabry's disease and occurs in 76.9% of females and 73.1% of males. As with medication use, VK is asymptomatic in Fabry's disease and its presence is not associated with more severe systemic disease (Sodi et al. 2007).

Classification

There is no specific classification for vortex VK. However, based on etiology, it can be classified as acquired or inherited.

Cross-References

- ▶ Chloroquine Toxicity, Cornea Verticillata
- ▶ Chlorpromazine, Cornea Verticillata
- ▶ Cornea Verticillata

References

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Vortex Keratopathy

- ▶ Cornea Verticillata
- ▶ Hurricane (Vortex) Keratopathy

W

Waardenburg-Jonkers Corneal Dystrophy

► Thiel-Behnke Dystrophy

Wallenberg Syndrome

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Synonyms

Lateral medullary syndrome; Posterior inferior cerebellar artery syndrome

Definition

Wallenberg syndrome (WS) is a clinical brainstem syndrome that is typically due to an ischemic infarction of the lateral medulla, often associated with a vascular lesion of the posterior inferior cerebellar arteries (PICA) and/or vertebral arteries. Medullary structures affected include spinothalamic tracts, spinal nucleus/tract of trigeminal nerve, nucleus ambiguous, vestibular nuclei, and ascending/descending autonomic fibers (Horner syndrome) (Larner 2006; Siegel et al. 2006; Walsh and Hoyt's 2008).

Etiology

Although ischemia is the classic etiology of WS, tumor, demyelination, and trauma can produce

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brainstem symptoms and signs of the WS (Walsh and Hoyt's 2008).

Clinical Presentation

Symptoms and signs of the WS include the classically described crossed signs of contralateral loss of pain and temperature in the body and ipsilateral face, loss of coordination, loss of gag reflex, hoarseness, dizziness, nausea, nystagmus, and difficulty with speech and swallowing. Lateropulsion (i.e., the sensation of being pulled toward one side, usually on the side of lesion) is often described. Uncontrollable hiccups may also be present, and problems with gait and balance coordination may also occur. Differences in heart rate and blood pressure from autonomic dysfunction may also be noted (Larner 2006; Siegel et al. 2006; Walsh and Hoyt's 2008).

Diagnosis

The diagnosis of WS is a clinical one supported by radiographic findings (e.g., computed tomography (CT) or magnetic resonance imaging (MRI)) (Brazis et al. 2007; Arora et al. 2011).

Differential Diagnosis

Horner syndrome
  Brainstem neoplasm

Therapy

Treatment is mainly supportive and directed at the etiology.

Prognosis

Prognosis depends upon the etiology and the size and location of brainstem lesion if damaged by stroke (Brazis et al. 2007; Arora et al. 2011).

Epidemiology

WS affects less than 200,000 people in the United States.

Cross-References

▶ Idiopathic Facial Paralysis

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Wart

▶ Human Papilloma Viruses, Ocular Infection

Watershed Zone of the Choroid

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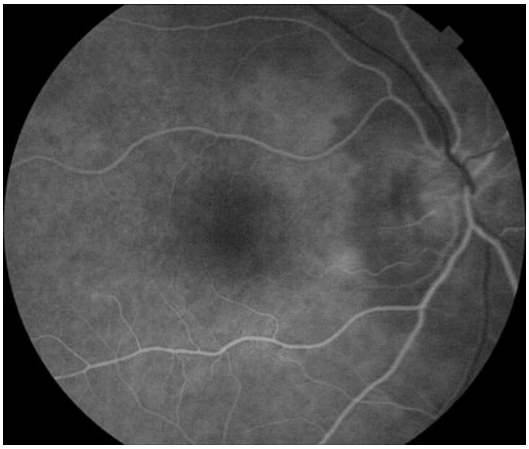
Definition

Watershed zone of the choroid is the anatomic region of choroid variably located between fovea and nasal edge of the optic nerve that represents



Watershed Zone of the Choroid, Fig. 1 Fluorescein angiography demonstrating choroidal watershed zone as hypofluorescent stripe between optic nerve and fovea

border of choroidal perfusion between temporal and nasal posterior ciliary arteries. This area can be identified as a transient vertical hypofluorescent stripe during the early choroidal phase of fluorescein or indocyanine green angiography (Johnson et al. 2006) (Fig. 1).

Cross-References

- ▶ Angiography, Fluorescein
- ▶ Communicating Arteries Anterior
- ▶ Fluorescein, as Diagnostic Agent

References

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Wave Front Aberrometry

- ▶ Wave Front Analysis

Wave Front Analysis

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Synonyms

Aberrometry; Corneal aberrometry; Wave front aberrometry

Definition

Wave front analysis is a general descriptor for a number of methods used to quantify and analyze the optical quality of an optical system such as the eye.

Purpose

The goal of wave front analysis, as it relates to ophthalmology, is to analyze the optical quality of the eye. This information can then be used to guide treatment, for instance, with laser refractive surgery, assist in diagnosis of subjective visual quality complaints, or investigate the affects of various parameters on the quality of the optical system of the eye, for instance, in dry eye (Mello et al. 2012).

Principle

In the context of wave front analysis, the optical quality of an eye is measured as the degree to which the eye in question deviates from an ideal optical system. This deviation is often referred to as aberration or a wave front error. An aberrometer acquires this wave front error data and uses a mathematical equation to separate this wave front error into its component parts. In order to separate the wave front error into its component parts, mathematical analysis is undertaken, usually with polynomial equations such as the Zernike polynomial equation. Zernike polynomials deconstruct the wave front

error into different orders each representing a different type of aberration. For example, lower-order aberrations such as second-order aberrations include the familiar sphere and regular astigmatism errors. Higher-order aberrations include aberrations like coma and trefoil (third-order aberrations) or spherical aberration, secondary astigmatism, and tetrafoil (fourth-order aberrations) (Maeda 2009).

It is important to note that currently used aberrometers measure only monochromatic aberrations and do not address scatter, diffraction, and chromatic aberration (Zuberbuhler et al. 2013).

Indication

There are a number of applications for which wave front analysis has been employed. One of the most common and well-known applications for wave front technology is in guiding excimer laser ablation in refractive surgery. Wave front analysis has been used in this setting to both reduce preexisting aberrations as well as to avoid introducing new errors during ablation.

One important distinction to recognize in this area is the difference between wave front-guided and wave front-optimized treatments. Wave front-guided treatments rely on wave front measurements of the individual patients' higher-order aberrations to create a unique ablation profile for treatment of that particular patient's high- and low-order aberrations. Wave front-optimized treatments attempt to diminish aberrations by applying a precalculated aspheric treatment profile for a particular sphero-cylindrical refraction.

Other indications for wave front analysis include evaluating patients with keratoconus or pellucid marginal degeneration, cataracts and intraocular lenses as well as investigating tear film dynamics and the effects of ageing on the cornea (Maeda 2009; Mello et al. 2012).

Contraindications

There are no true contraindications to the use of wave front analysis, but there are certain limitations to the use of these technologies. Currently available wave front sensors are fairly accurate with low and moderate amounts of higher-order aberrations, but extreme levels of aberrations are not able to be measured accurately. Additionally, various factors related to the eye being evaluated may make measurements more or less accurate. For example, patients with dry eyes or poor tear films can have increased aberrations. The pupil size and presence of cataract can significantly alter measured aberrations. Multifocal intraocular lenses can also lead to errors in measurements of ocular aberrations (Mello et al. 2012).

Advantage/Disadvantage

The primary advantage of wave front technology lies in its ability to measure higher-order aberrations. These measurements can then be used to tailor refractive treatments in order to minimize the presence and effects of these aberrations on the patients' vision. This technology can also be used to evaluate the quality of the optical system in order to diagnose issues that may lead to poor image quality that could previously not be explained or detected (Oliveira et al. 2012).

Although wave front technology for refractive surgery can help in creating an optimal plan for treatment, at least in regard to certain optical aberrations, it does not predict healing responses and their effect on posttreatment aberrations. As mentioned previously, currently used wave front technology uses one wavelength of light to make measurements therefore and only evaluate monochromatic aberrations and do not address scatter, diffraction, and chromatic aberration. In addition, as mentioned above, there are certain aspects of the eyes being evaluated such as cataract, multifocal intraocular lenses, etc. that limit the accuracy of wave front analysis (Oliveira et al. 2012).

Cross-References

▶ Computerized Corneal Topography
▶ Holmium YAG Laser, Thermokeratoplasty

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Wavefront Aberration Coefficients

▶ Zernike Coefficients

Wavefront Measurement

▶ Aberrometry

Wavefront Sensing

▶ Aberrometry

Wavefront-Guided Laser In Situ Keratomileusis

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Synonyms

Custom LASIK; Wavefront-guided LASIK; wg-LASIK

Basic Characteristics

Excimer laser keratorefractive surgery such as photorefractive keratectomy (PRK) or laser in situ keratomileusis (LASIK) successfully reduces sphero-cylindrical refractive errors, also known as lower-order aberrations (LOA). Wavefront-guided ablation profiles incorporate also the treatment of higher-order aberrations (HOA) which are present in the normal eye (Salmon and van de Pol 2006). Therefore, the treatment is not solely based on subjective refraction data but also on measurements obtained with a wavefront sensor (aberrometer). Subjective refraction values and HOA, often also corneal height data, are merged into an ablation profile that aims at reduction of both LOA and HOA. The first wg-LASIK treatment was performed by Seiler in 1999 (Seiler et al. 2000). Subsequently, numerous laser platforms for wavefront guided treatments including aberrometer and excimer laser became commercially available.

The benefit of wg-LASIK over conventional (sphero-cylindrical) LASIK is judged controversially. First-generation algorithms had a limited predictability of HOA reduction because induced HOA overrode the reduction effect (Kohnen et al. 2004; Bühren and Kohnen 2006). Later enhancements like improved eye trackers, faster excimer lasers, aspheric ablation profiles, and the use of femtosecond lasers for flap creation led to better results.

After one decade, the overall benefit of wg-LASIK is discussed controversially. On one hand, large studies showed (a moderate) superiority of wg-LASIK (Schallhorn et al. 2008), on the other hand, the effect of physiological HOA on retinal image quality is rather negligible (Yoon and Williams 2002), in particular in the context of HOA induction by the procedure itself.

Wavefront-guided ablations can also be performed with surface ablation techniques. Similar to wg-LASIK is topography-guided LASIK which is primarily used for secondary treatments of highly aberrated eyes, e.g., after decentration of the optical zone.

Cross-References

▶ Aspheric Ablation Profile
▶ Custom LASIK
▶ Excimer Lasers
▶ Wavefront-Guided LASIK

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Wavefront-Guided Laser Refractive Surgery

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See "► Wavefront-Guided Laser In Situ Keratomileusis".

Wavefront-Guided LASIK

► Wavefront-Guided Laser In Situ Keratomileusis

Wavefront-Optimized Ablation Profile

► Aspheric Profile Photorefractive Keratectomy
► Q-Factor Customized Ablation Profile

Wavelength-Dependent Refractive Index

► Dispersion: Definition

WEBINO

► WEBINO ("Wall-Eyed" Bilateral Internuclear Ophthalmoplegia) Syndrome

WEBINO ("Wall-Eyed" Bilateral Internuclear Ophthalmoplegia) Syndrome

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Synonyms

WEBINO

Definition

Wall-eyed bilateral internuclear ophthalmoplegia (WEBINO) is a disorder often characterized by primary gaze exotropia and a bilateral adduction

deficit with a dissociated, horizontal abducting-eye nystagmus in horizontal gaze.

Etiology

This disorder is typically caused by a lesion involving both medial longitudinal fasciculi (MLF). Breakdown of fusional mechanisms results in the concomitant exotropia (i.e., "wall eyed").

Occurrence

WEBINO occurs most frequently in patients with multiple sclerosis or brainstem strokes, but any lesion of bilateral MLF can produce a clinical WEBINO. Myasthenia gravis can also mimic WEBINO (i.e., "pseudo-INO").

Cross-References

- ▶ Internuclear Ophthalmoplegia
- ▶ One-and-a-Half Syndrome
- ▶ Ophthalmoplegia, Internuclear

Further Reading

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Wegener Granulomatosis

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Definition

Wegener's granulomatosis (WG) is noninfectious systemic vasculitis that typically involves the respiratory tracts and kidneys (Pakrou et al. 2006). Orbital and ocular adnexal involvement occurs in up to 50% of patients and can include all ocular tissues (Pakrou et al. 2006; Perez et al. 2004).

Background

Scottish otolaryngologist Peter McBride (1854–1946) first described the condition in 1897, and it was later refined by Friedrich Wegener (1907–1990), a German pathologist in 1936 and 1939 (Bhatia et al. 2005). Classic and limited forms of WG have been recognized. Classic WG is a multisystem disorder that shows upper and lower respiratory tract granulomas, generalized vasculitis, and glomerulonephritis. The limited form does not always progress to generalized disease, often does not affect the kidneys, usually involves the head and neck, and is associated with a better prognosis. Orbital and adnexal manifestations can occur in either form.

Etiology/Pathophysiology

Wegener's granulomatosis (WG) results from the dual contributions of type II (cytotoxic) and Coombs hypersensitivity reactions giving rise to antibodies to neutrophil cytoplasmic antigens (ANCA) and type IV (cell-mediated) reaction leading to formation of giant cells and granulomas (Fechner et al. 2002). The disease involves small-sized, more often than medium-sized, blood vessels. Disease complications may result from focal vasculitis, granulomatous inflammation, vascular thrombosis, and hemorrhage, or due to chronic inflammation or ischemia (Perez et al. 2004). Orbital and adnexal disease accounts for a significant portion of ocular involvement. Orbital involvement may be due to either primary inflammation or result from contiguous extension of disease from adjacent paranasal sinuses or nasopharynx (Fechner et al. 2002).

Epidemiology

WG demonstrates a strong predominance for Caucasians, particularly those of northern European

ancestry, and affects males and females equally. The annual incidence is estimated to be approximately ten cases per million, and the mean age at diagnosis is 50 years. Orbital involvement occurs in up to 50% of patients (Perez et al. 2004).

Clinical Presentation

Ocular involvement in WG is reported to be the presenting feature in up to 15% of patients (Pakrou et al. 2006). Orbital disease usually manifests as proptosis, ocular pain, epiphora, or injection. Many patients may also develop diplopia, which may be due to the mass effect itself or vasculitis of vessels supplying the extraocular muscles (Fechner et al. 2002). The features of orbital disease are frequently bilateral and constitute a severe risk to useful vision, secondary to optic nerve compression or proptosis with associated exposure keratopathy. Orbital socket contracture is also a reported complication and represents proliferation of fibrous tissue replacing areas of acute inflammation and necrosis.

Diagnosis

The diagnosis of orbital WG depends on a combination of clinical and serological findings. However, given the overlap in presentation with other entities, biopsy remains indispensable. The histopathologic triad of granulomatous inflammation, tissue necrosis, and vasculitis is seen in less than 50% of orbital biopsies (Perez et al. 2004; Fechner et al. 2002).

ANCA is not recommended to be used alone in place of a biopsy because ANCA is positive in less than 70% of cases of limited WG. Positive ANCA may help in establishing the diagnosis in cases in which typical pathological features are lacking, and it has a value in following disease activity.

With respect to diagnostic imaging, although computed tomography can reveal sinus structure involvement and an orbital mass, MRI can depict granulomas and better delineate mucosal inflammation and ulceration in the sinuses, nasal cavity, and orbits.

Differential Diagnosis

Bacterial or fungal orbital inflammatory infiltration
Lymphoma of the orbit
Sarcoidosis
Graves orbitopathy
Idiopathic orbital inflammation (orbital pseudotumor)

Treatment

The gold standard treatment for WG and ANCA-associated vasculitis combines glucocorticoids and cyclophosphamide (Pakrou et al. 2006). In cases of limited WG, an alternative regimen of methotrexate and glucocorticoids may also be used. In general, appropriate treatment of the underlying disease is satisfactory in managing associated ocular problems. Surgical interventions in the management of WG are largely limited to those involved with obtaining tissue biopsies for pathological analysis. However, in cases of nasolacrimal duct obstruction, dacryocystorhinostomy can be effective.

Prognosis

Limited WG of the orbit is a rare disease but with overall good prognosis (Bhatia et al. 2005). In all cases of WG, early recognition and referral to a trained specialist, accompanied by prompt treatment and periodic follow-up, can significantly decrease the risk of visual impairment.

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Weill-Marchesani Syndrome

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Synonyms

Mesodermal dysmorphodystrophy, congenital; Spherophakia-brachymorphia syndrome

Definition

Weill-Marchesani syndrome (WMS) is a rare inherited disorder of connective tissue first described by Weill in 1932 and further delineated by Marchesani in 1939 (Faivre et al. 2003). It is characterized by proportionate short stature, brachydactyly, joint stiffness, broad skull, heart defects, and characteristic eye abnormalities including shallow orbits, microspherophakia (small spherical lens), ectopia lentis (abnormal position of the lens), high myopia, and glaucoma.

Etiology

Weill-Marchesani syndrome is an inherited disorder of the connective tissue. Two modes of inheritance are predominant, the autosomal dominant (45%) and the autosomal recessive (39%), but there are also 16% of simplex cases (single occurrence in a family). For the autosomal recessive form, mutations in ADAMTS10 gene located on chromosome 19 (19p13.3-p13.2) have been shown (Tsilou and McDonald 2007). The product of the gene ADAMTS10 (disintegrin-like and metalloproteinase with thrombospondin type 1 motif) belongs to the ADAMTS family of proteins, believed to be anchored to the extracellular matrix. Mutations in FBN1 were found in a large family with autosomal dominant WMS.

Clinical Presentation

WMS usually presents in childhood with short stature and/or ocular problems. The mean age of recognition of an ocular problem is 7.5 years. Microspherophakia is the most important manifestation of WMS. Microspherophakia results in lenticular myopia, which is usually the first ophthalmological finding. Ectopia lentis usually results in downward displacement of the lens. Glaucoma is the most serious complication and results in most cases by pupillary block because of forward movement of the lens or by dislocation of the lens into the anterior chamber (Ritch et al. 2003). Chamber angle abnormalities have also been described. Biometry in eyes of patients with WMS shows thicker cornea, higher keratometry values with usually oblique astigmatism, shorter axial length, shallower anterior chamber, and thicker lens than age-matched normals.

Loss of vision occurs earlier in WMS and is more severe than in other lens dislocation syndromes. In some cases, lens dislocation and pupillary block appear after blunt trauma to the eye weakens the zonular fibers. Presenile vitreous liquefaction has been described in a large family with autosomal dominant WMS.

Proportional short stature is an essential part of the syndrome. An adult male with WMS is expected to achieve a height of 142–169 cm, while an adult female is expected to achieve a height of 130–157 cm. Digits are short (brachydactyly) and joints are stiff. Heart abnormalities are occasionally seen and include patent ductus arteriosus and pulmonary stenosis. Some of the WMS patients show mild to moderate mental retardation.

Diagnostics

Diagnostic criteria for WMS have not been formally established. The clinical diagnosis of WMS

is considered when the key findings of ocular abnormalities (microspherophakia and ectopia lentis), short stature, brachydactyly, joint stiffness, and heart defects (occasional) are observed. Establishing the diagnosis in a proband relies on clinical findings, but molecular genetic testing of the ADAMTS10 sequence variants can help confirm the diagnosis.

Differential Diagnosis

Ectopia lentis can also occur in Marfan syndrome, homocystinuria, sulfite oxidase deficiency, and hyperlysinemia. All, however, are clinically distinct from WMS. Simple dominant ectopia lentis, ectopia lentis and pupillae have ocular findings only, and glaucoma-lens ectopia-microspherophakia-stiffness-shortness (GEMSS) syndrome has features resembling WMS (WMS-like syndrome).

Prophylaxis

In an inherited disease, there is no primary prophylaxis available. In affected individuals periodic ophthalmic examinations for early detection and removal of an ectopic lens can help decrease the possibility of pupillary block and glaucoma. Airway management during general anesthesia can be difficult in persons with WMS because of the stiff joints, poorly aligned teeth, and maxillary hypoplasia. Patients with WMS should have a clinical cardiology evaluation including ECG and baseline echographic examination to rule out occasional heart defects.

Therapy

Correction of progressive high myopia to improve vision is the primary goal of treatment when WMS is detected in a young person. Implantation of phakic anterior chamber lenses to correct myopia is contraindicated. If the anterior chamber is very shallow, the lens rather thick and/or subluxated, and signs of imminent pupillary block or anterior synechia are present, laser or surgical iridectomy/iridotomy should be performed as prophylaxis of pupillary block glaucoma. Use of ophthalmic miotics and mydriatics should be avoided as they can induce pupillary block. If iridotomy/iridectomy fails to open the angle and appositional angle closure persists, argon laser peripheral iridoplasty (ALPI) might be successful. Surgery for ectopic lenses should not be delayed as patients may develop acute angle closure when the lens spontaneously or following minor ocular trauma luxates into the anterior chamber. Pars plana lensectomy or extraction of the lens via anterior approach including anterior vitrectomy should be performed (Harasymowycz and Wilson 2004). For an experienced surgeon, stabilization of the capsular bag using modified capsular tension rings may allow to implant a posterior chamber lens (Cionni et al. 2003).

Prognosis

Life expectancy is not limited by the disease. If angle-closure glaucoma is diagnosed early enough and treated adequately and the lens is removed if required, visual prognosis may only be limited by some degree of ametropic amblyopia. If angle closure is the presenting sign, urgent surgery may be required.

Epidemiology

The exact incidence of WMS is not known, but it is a rare disease. In 2003 Faivre et al. reviewed 128 cases from the literature.

Cross-References

- ▶ Angle-Closure Glaucoma
- ▶ Ectopia Lentis
- ▶ Lens-Induced Angle-Closure Glaucoma

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Welder's Flash or Arc Eye

▶ Arc Welding, Occupational Light Injury and

Welders Maculopathy

▶ Arc Welding, Occupational Light Injury and

wg-LASIK

▶ Wavefront-Guided Laser In Situ Keratomileusis

White-to-White Distance

▶ Corneal Diameter

Whitnall's Ligament

▶ Superior Transverse Ligament

Wies Procedure

▶ Tarsotomy

Wies Repair

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Synonyms

Transverse tarsotomy; Two-snip procedure

Definition

The Wies repair is a surgical technique used in the repair of eyelid entropion that was initially described by Frederic Wies in 1954 (Wies 1954). It involves the creation of a full-thickness lower eyelid horizontal incision to negate upward movement of the preseptal orbicularis muscle over the tarsal plate, as well as the placement of horizontal mattress sutures that evert the eyelid margin.

Indication

The Wies repair is a relatively simple surgical procedure that has been shown to be relatively effective in cases of eyelid entropion. It has been described in the surgical repair of both involutional and cicatricial ectropion. The full-thickness lower eyelid horizontal incision leads to the development of fibrous scar tissue that acts as a barrier preventing the upward movement or overriding of the preseptal orbicularis muscle.

Contraindication

Contraindications to the Wies repair, which is usually performed under general anesthesia, are generally related to the general medical condition and operative risk of the patient. The Wies repair may be contraindicated in patients with concurrent uncontrolled medical conditions, systemic anticoagulation, or other conditions that interfere with appropriate positioning or safe management of the patient in the operating room. In such situations, simpler less invasive methods of eyelid malposition correction such as the Quickert procedure for entropion may be preferred, even if they may be associated with higher long-term recurrence.

Techniques and Principles

1. After skin preparation, infiltrate locally administered anesthetic agent subcutaneously and subconjunctivally along the inferior border of the tarsus.
2. Use a 15 blade to make a full-thickness incision through the middle lower eyelid at the level of the lower tarsus, approximately 2–3 mm below the lower eyelid margin. Utilize a corneal shield to protect the globe prior to performing the skin incision.
3. Starting from the conjunctival aspect of the lower eyelid margin, pass each arm of a 5–0 double-armed suture (e.g., Vicryl) full-thickness through the eyelid just inferior to the inferior margin of the full-thickness eyelid incision.
4. Pass each arm of the double-armed suture through the eyelid superior to the full-thickness incision in a partial thickness fashion, exiting the eyelid just inferior to the lash line.
5. Tie both ends of the double-armed suture together to complete the horizontal mattress suture.
6. Repeat steps 3–5 two to three more times to complete closure of the full-thickness eyelid incision.

The Wies procedure is also referred to as the two-snip procedure due to the nature in which the full-thickness eyelid incision may be made by extending a full-thickness stab wound with two scissor snips nasally and temporally.

Outcome

The Wies procedure is reported to have unsatisfactory surgical outcome rates as low as 11% (Lance and Wilkins 1991) and as high as 48% (Boboridis et al. 2000). The Wies repair alone does not address horizontal or vertical eyelid laxity and has been unfavorably compared to other procedures like the tarsal strip procedure that do so with higher reported surgical success rates. When combined with a lateral tarsal shortening procedure, surgical outcomes generally improved (Lance and Wilkins 1991). Nevertheless, in a direct comparison between procedures that did not involve horizontal shortening of the lower eyelid, the Wies repair was also found to be inferior to the Jones' retractor plication procedure (Boboridis et al. 2000).

The Wies repair has also been reported to be associated with higher rates of consecutive ectropion, which may be a result of cicatricial changes associated with the full-thickness eyelid incision inherent in the procedure (Baylis et al. 1977; Cheung and Sandramouli 2004). The process of cicatricial scarring is difficult to predict and is itself a known cause of eyelid entropion and ectropion.

Complications

Complications of the Wies repair include failure of entropion correction, recurrence, ectropion overcorrection, granuloma formation, infection, bleeding, and wound dehiscence. Careful burying of deep sutures while minimizing dead space aids in the reduction of suture granuloma formation and suture extrusion. Attention to appropriate surgical technique, good placement of sutures, and knot security maximizes the chances of surgical success. Avoidance of trauma in the postoperative period, good patient hygiene, and use of topical antibiotic ointment may also contribute to minimizing complications.

Cross-References

- ▶ Congenital Entropion
- ▶ Sutures (Surgical), Quickert, for Involutional Entropion
- ▶ Tarsal Strip Procedure

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Wilbrand Knee

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Synonyms

Junctional scotoma; Optic nerve decussation

Definition

The so-called Wilbrand knee is an anatomical term that describes decussating optic nerve fibers discovered by Hermann Wilbrand in 1904 (Wilbrand et al. 1904). He studied cadavers that had undergone enucleation prior to death and found inferonasal nerve fibers that looped into the contralateral optic nerve prior to traveling in the optic tract (Wilbrand et al. 1904). He believed these fibers would result in a pattern of vision loss seen with some parasellar lesions causing compression of the inferonasal optic nerve at its junction with the optic chiasm, namely, a central scotoma in the ipsilateral eye and a smaller superior temporal hemianopia in the contralateral eye (from involvement of the crossing inferonasal fibers) (Lee et al. 2006).

In 1997 JC Horton reported that the Wilbrand knee was actually an artifact of optic nerve atrophy after enucleation in monkeys (Horton 1997). He studied three postmortem human optic chiasms that had undergone monocular enucleation at time points of 5 months, 27 months, and 28 years prior to death and concluded the same was true for humans. It is now believed that shrinkage of the optic nerve in the enucleated eye causes the contralateral optic nerve to briefly enter the atrophic nerve resulting in a classic Wilbrand knee (Horton 1997).

In 2006 Lee et al. presented three cases of optic nerve lesions near the optic chiasm requiring resection. In all three cases, resection of the diseased optic nerve was performed without loss of vision in the contralateral eye, supporting the belief that Wilbrand knee is not found in normal human patients (Lee et al. 2006). Despite the anatomic controversy, the localizing value of the clinical visual field defect known as the junctional scotoma (ipsilateral nerve fiber layer defect or central scotoma and contralateral superotemporal visual field loss) is still localizing to the junction of the optic nerve and chiasm.

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Wilson Disease

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Synonyms

Hepatolenticular degeneration

Definition

Wilson disease is a genetic disorder of systemic copper accumulation. It is due to defective hepatic excretion and characterized by progressive neurologic disease, chronic liver disease, and ocular manifestations including Kayser-Fleischer rings and "sunflower" cataracts (Yanoff and Duker 2009; Kanski and Bowling 2011; Krachmer et al. 2011).

Etiology

Copper deposition in Wilson disease occurs due to decreased biliary copper excretion and diminished copper uptake into ceruloplasmin transport protein. An autosomal recessive mutation in *ATP7B* (13q14.3–q21.1), which codes for intrahepatocytic transport proteins necessary for ceruloplasmin copper uptake mechanism, is responsible for disease. Systemically, this process leads to development of liver failure and neurologic deficits as a result of copper accumulation in basal ganglia (Yanoff and Duker 2009; Kanski and Bowling 2011; Krachmer et al. 2011).

Clinical Presentation

The Kayser-Fleischer ring is a peripheral orange, brown, or green-brown discoloration due to gradual copper accumulation at the level of the Descemet membrane adjacent to the limbus. Approximately 95% of patients with neurologically symptomatic Wilson disease initially present with a Kayser-Fleischer ring in the peripheral cornea. This begins primarily in superior and inferior arcs which eventually coalesce to form a 360° green-brown zone of copper granule deposits in the Descemet membrane. Copper accumulation begins peripherally at Schwalbe's line and moves centrally. Slit-lamp biomicroscopy is used to identify these rings in most instances. Gonioscopy may be required to locate the ring in its early stage due to its primary peripheral location.

Copper accumulation within the lens capsule results in "sunflower" cataract, present in approximately one in five patients with neurologically symptomatic Wilson disease. This is characterized by multicolored central opacities with radiating spokes beneath the lens' anterior and posterior capsule. These cataracts occur in small portion of patients and do not impair vision. They may disappear within a few years of starting chelating therapy.

Systemically, patients may present with earlier symptom of jaundice indicating onset of liver disease. Basal ganglia dysfunction, behavioral disturbances, and nephrotic syndrome may manifest due to systemic copper toxicity (Yanoff and Duker 2009; Kanski and Bowling 2011; Krachmer et al. 2011).

Diagnosis

Diagnosis of Wilson disease is multifactorial and relies on the presence of characteristic clinical features and biochemical parameters. In a majority of patients, the presence of a Kayser-Fleischer ring and a low serum ceruloplasmin level (<200 mg/L) is sufficient to establish a diagnosis. In patients with neurological signs or symptoms, diagnosis can be made from the presence of

Kayser-Fleischer rings alone. Subsequent MRI scans may show lesions at sites compatible with the neurological features. Other biochemical findings include elevated basal 24-h urinary copper excretion and increased hepatic parenchymal copper concentration. In the absence of Kayser-Fleischer rings or neurologic dysfunction, a liver biopsy for quantitative copper measurement is necessary to establish diagnosis (Yanoff and Duker 2009; Kanski and Bowling 2011; Krachmer et al. 2011).

Differential Diagnosis

Corneal chalcosis (corneal copper deposition) may also occur due to intraocular foreign body, chronic copper poisoning, and multiple myeloma. Based on systemic presentation of Wilson disease, relevant neurologic and hepatic diagnoses should be considered such as cirrhosis, hepatitis, and neurodegenerative disease (Yanoff and Duker 2009; Kanski and Bowling 2011; Krachmer et al. 2011).

Prophylaxis

There are currently no methods of primary prophylaxis for Wilson disease. Genetic counseling is recommended for individuals with a family history of Wilson disease (Yanoff and Duker 2009; Kanski and Bowling 2011; Krachmer et al. 2011).

Therapy

Medical management of Wilson disease addresses systemic excess of copper through increased excretion and decreased absorption. Systemic copper removal is attained by D-penicillamine, a chelating agent. Zinc is administered to interfere with intestinal copper uptake and stabilize hepatic copper through the induction of metallothioneins. Patients are recommended to avoid foods with high copper content. Lifelong treatment is required to prevent further complications. Ocular examination can be utilized to assess the reduction of systemic copper levels (Yanoff and Duker 2009; Kanski and Bowling 2011; Krachmer et al. 2011).

Prognosis

Patient outcome in Wilson disease is optimized if treatment is started soon after disease is diagnosed. Failure to adhere to a consistent treatment regimen may result in loss of liver function and neurologic damage. Rapid hepatic decompensation may occur within three years and as early as eight months after treatment is stopped. Liver damage is usually refractory to reinstitution of chelation therapy. Affected patients require liver transplantation (Yanoff and Duker 2009; Kanski and Bowling 2011; Krachmer et al. 2011).

Epidemiology

Wilson disease occurs on average in 1 in 30,000 individuals, with a corresponding carrier frequency of 1 in 90. Prevalence is increased among Sardinian and Chinese populations (1 in 10,000). It is relatively infrequent in individuals of African descent (Yanoff and Duker 2009; Kanski and Bowling 2011; Krachmer et al. 2011).

Cross-References

▶ Kayser-Fleischer Ring

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Word Blindness

▶ Alexia, Without Agraphia

Wound Healing

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Definition

Biological response of the cornea to (surgical) trauma.

Function

Surgical epithelial defects (induced by alcohol in LASEK, mechanical scrape in PRK, microkeratome or femtosecond laser application in LASIK and Epi-LASIK) lead to a release of cytokines from the injured epithelium. These cytokines and cytokines from the tear film induce apoptosis and necrosis of keratocytes in the anterior corneal stroma. Proinflammatory cytokines attract macrophages, T cells, and polymorphonuclear cells arriving via the limbal vessels and from the tear film. These cells clear cell debris. Remaining keratocytes from the deeper stroma are subsequently activated, proliferate, migrate, and repopulate the depleted stroma. Myofibroblasts derived form keratocytes responding to TGF ß play a role in stromal remodeling due to collagen and extracellular matrix formation. Myofibroblasts have a lower transparency than normal keratocytes due to a lower concentration of corneal crystallines in their cell body. Myofibroblasts play an important role in haze formation and regression. With the formation of a functional basement membrane myofibroblasts slowly disappear over months. Corneal wound healing processes are more pronounced after surface ablation as compared to LASIK because of the disruption of the epithelial basement membrane over the central cornea. In LASIK, wound healing processes are mainly limited to the cut margins and the corneal stroma adjacent to the flap interface. However, a significant decrease in keratocyte density in the flap and anterior subablation zone over the postoperative years has been observed after LASIK, but the clinical significance of this finding remains unclear. The decrease in keratocyte density may be associated with the trauma to stromal corneal nerves in LASIK surgery. Refractive regression, especially in higher levels of corrections, is more common and more pronounced after surface ablation than after LASIK. Refractive regression is associated with thickness changes in the cornea due to stromal remodeling and epithelial hyperplasia.

Clinical Relevance

Corneal wound healing after surgical trauma is aimed at restoring corneal hemostasis, barrier function, and corneal transparency. However, corneal wound healing processes are associated with refractive regression and haze formation, especially in surface ablation procedures.

Cross-References

- ▶ Corneal Ablation
- ▶ Corneal Stromal Haze
- ▶ Custom LASIK

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X

Xanthelasma

► Epidermal Cysts, of the Eyelid
► Xanthomas

Xanthelasma Palpebrarum

► Xanthomas

Xanthelasma, Dyslipoproteinemia

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Synonyms

Planar xanthoma

Definition

Xanthelasmas are single or multiple soft, flat or slightly elevated, yellowish plaques on the eyelids or in the periorbital skin, particularly, near the inner canthi (Weedon 2010; Eagle 2011).

Histologically, xanthelasmas are characterized by sheets of foamy, lipid-laden histiocytes within the upper dermis, often around blood vessels as well as the pilosebaceous follicles (Weedon 2010) (Fig. 1).

Etiology

Although abnormal lipid metabolism has been described to play an important role in the development of xanthelasmas, approximately 50% of cases have normal lipids (Rohrich et al. 2002; Weedon 2010; Eagle 2011). The pathogenesis remains unclear; apoprotein abnormalities and vascular permeability impairment have been documented as contributing factors (Weedon 2010).

Clinical Presentation

Typically, xanthelasmas present as yellow, soft macules or slightly elevated plaques on the medial aspect of the upper and lower eyelids (Fig. 2).

In children, the presence of corneal arcus as well as extensor tendon xanthomas, and associated xanthelasmas, is always a sign of hyperlipoproteinemia (Rohrich et al. 2002).

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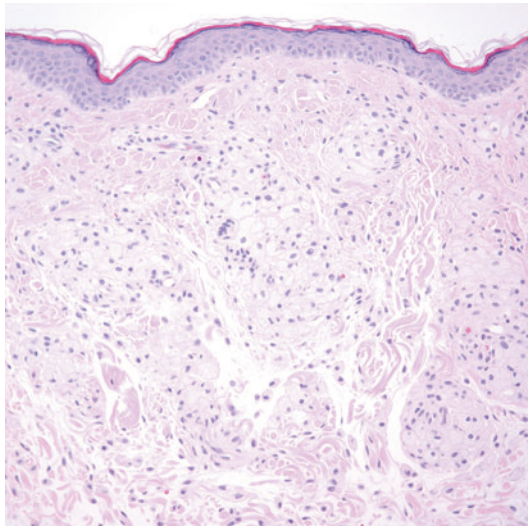
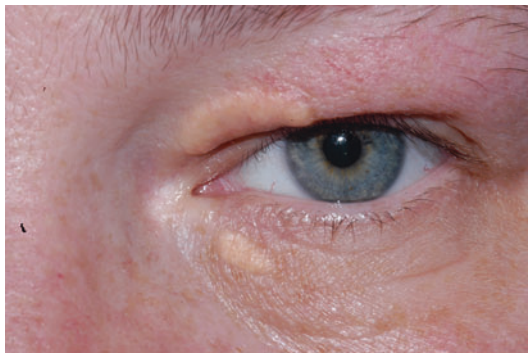


Xanthelasma, Dyslipoproteinemia, Fig. 1 Histologic section of xanthelasma, intradermal foamy macrophagees, H&E 100X



Xanthelasma, Dyslipoproteinemia, Fig. 2 Xanthelasmas in the nasal aspect of upper and lower lids

Diagnosis

In general, xanthelasmas are diagnosed clinically and its presence may be an important factor of underlying systemic disease (Rohrich et al. 2002; Weedon 2010; Eagle 2011). If they present before age 40, association with familial dyslipoproteinemia including type IIa, IIb, and even type III needs to be considered, and a lipid profile is recommended (Rohrich et al. 2002).

Differential Diagnosis

Other systemic conditions such as cirrhosis, hypothyroidism, and nephrotic syndrome need to be also considered as part of the differential diagnosis for typical lesions (Rohrich et al. 2002; Weedon 2010; Eagle 2011).

More severe xanthogranulomatous disorders such as necrobiotic granuloma, orbital xanthogranuloma with adult onset, and Erdheim-Chester present with atypical indurated xanthelasma-like lesions (Rohrich et al. 2002; Eagle 2011). Lipoid proteinosis, a very rare autosomal recessive disorder which is characterized by perivascular deposits of hyaline, may present as well, with very similar atypical lesions along the lid margin (Rohrich et al. 2002).

Prophylaxis

No definitive alternatives to prevent the development of xanthelasma have been described yet. However, dietary restriction of fat has been associated with xanthelasma regression (Rohrich et al. 2002). As before, treatment of the underlying disease may also cause regression of the lesion as seen when hormone replacement therapy is given such as in hypothyroidism (Caplan and Curtis 1961; Rohrich et al. 2002).

Therapy

In general, xanthelasma represents a cosmetic concern and very rarely may obstruct visual axis due to its size (Rohrich et al. 2002). A variety of therapeutic options are considered in order to ameliorate the appearance of the eyelid including surgical excision; ablation with laser such as carbon dioxide, argon, and erbium-yttrium-argon-garnet (YAG); pulsed dye; peeling of the lesions with trichloroacetic acid; and also giving therapeutic agents for the underlying medical condition (Caplan and Curtis 1961; Mendelson and Masson 1976; Rohrich et al. 2002).

Prognosis

Overall, xanthelasma represents a benign condition which commonly recurs, regardless of the type of treatment (Rohrich et al. 2002; Weedon 2010; Eagle 2011). Mendelson and Masson (1976) previously found 40% recurrence rate after primary excision and 60% recurrence rate after secondary excision, having the highest incidence of recurrence, 26%, within the first year. They did also highlight three scenarios in which surgical excision is less likely to prevent lesion recurrence: patients with defined familiar hyperlipoproteinemia, involvement of all four eyelids, and more than one recurrence (Mendelson and Masson 1976; Rohrich et al. 2002).

Epidemiology

Xanthelasma is the most common cutaneous xanthoma (Weedon 2010) In general, most of the patients are in the fifth or sixth decade of life with an incidence of 1.1% in women and 0.3% in men (Caplan and Curtis 1961; Rohrich et al. 2002). Patients with a history of familial hypercholesterolemia may develop these lesions at a younger age (Caplan and Curtis 1961; Rohrich et al. 2002; Weedon 2010).

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Xanthomas

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Synonyms

Xanthelasma; Xanthelasma palpebrarum

Definition

Xanthomas are sharply demarcated, yellow-colored lesions in the connective tissue of skin, tendons, or fascia that are formed by foam cells. In the eyelids, they appear most commonly near the medial canthus.

Etiology

Xanthomas develop through increased local extravasation of lipids through the vascular wall into the surrounding interstitial space. Local macrophages and monocytes phagocytose the lipid particles, mostly low-density lipoprotein (LDL) complexes, through LDL receptors. LDLs undergo intracellular oxidation, which gives rise to foam cells.

Clinical Presentation

Xanthelasma typically present in middle age during the fifth and sixth decades of life. The lesions are typically painless and do not affect vision.

Diagnosis

Eyelid xanthomas are diagnosed clinically based on the presence of yellow-colored, demarcated plaques near the medial canthus. Biopsy is typically not warranted for diagnosis, and histology demonstrates foam cells in the middle and superficial layers of the dermis in a perivascular and

periadnexal distribution. Lipid profiles will be abnormal in approximately one-half of patients.

Differential Diagnosis

There are several benign and malignant lesions to consider in the differential for xanthomas of the eyelid.

Benign lesions: chalazion, hordeolum, molluscum contagiosum.

Malignant lesions: basal cell carcinoma, squamous cell carcinoma, sebaceous carcinoma, keratoacanthoma.

Prophylaxis

Pharmacologic control of serum cholesterol does not appear to affect the clinical course and outcomes of xanthomas, despite the association of these lesions with serum lipid profile.

Therapy

The literature has described several treatment options for xanthomas of the eyelid. These include surgical resection; ablation with various lasers such as Nd:YAG, erbium YAG, and CO_2; and trichloroacetic acid (TCA) peels. Each method is associated with its own set of drawbacks. Surgical resection is limited by scar and ectropion formation. Pigmentation and scarring can complicate chemical treatment with TCA, and laser treatment is mostly beneficial early-stage lesions. All treatment modalities have a high rate of recurrence, especially when multiple eyelids are involved.

Prognosis

Removal of eyelid xanthomas is complicated by a high rate of recurrence. Their presence can also be associated with the presence of xanthomas elsewhere on the body. As for association with systemic disease, a prospective cohort study in *BMJ* with data from the Copenhagen City Heart Study found an increased risk for myocardial infarction, ischemic heart disease, and early mortality. This effect was independent of the presence of an abnormal lipid profile. However, other studies have disagreed, and the link between xanthomas and cardiovascular disease remains inconclusive.

Epidemiology

Xanthomas of the eyelid occur in both men and women, with increasing prevalence in middle age.

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Xanthophylls

▶ Carotenoids (Xanthophylls)

Xeroderma Pigmentosum

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Definition

First described in 1874 by Hebra and Kaposi, xeroderma pigmentosum is a rare autosomal

recessive disorder with a genetic defect in the deoxyribonucleic acid (DNA) repair system that results in an early susceptibility to developing malignancies in sun-exposed skin and ocular structures. Clinically, xeroderma pigmentosum is characterized by extreme sensitivity to sunlight, photophobia, and pigmentary skin changes. Ocular findings are most prevalent in sun-exposed areas and can include ectropion, symblepharon, pterygium, conjunctivitis, conjunctival nevi, extreme dry eye, and corneal ulcers and opacification. Benign lid papillomas, corneal dysplasias, and ocular neoplasms such as squamous cell carcinoma, basal cell carcinoma, and melanomas are also much more frequent.

Neurological changes are found in 14–40% of patients with xeroderma pigmentosum. Motor impairment, peripheral neuropathy, and mental retardation have been reported and are thought to be secondary to increased neurodegeneration from DNA damage. Patients also have an increased risk of oral mucosa cancers and internal organ neoplasms including leukemia and central nervous system neoplasms.

Etiology

The nucleotide excision repair (NER) pathway of DNA repair for ultraviolet (UV)-light-induced DNA damage is a multi-step process that involves damage recognition, localized opening of the DNA double helix around the area of injury, excision of damaged DNA, and DNA-repair synthesis to replace removed DNA. Genetic mutations in genes involved in the nucleotide excision repair (NER) pathway of DNA repair that characterize xeroderma pigmentosum result in failure to remove UV-light-induced DNA damage, and mutations are replicated in the genome. These changes can result in the transformation of normal cells to malignant cells.

Clinical Presentation

Hypersensitivity to sunlight presents at a very early age. Serious sunburns can occur after very minimal sunlight exposure and persist for weeks. Significant pigmentary changes occur in light-exposed skin. Erythema, pigmentary changes, scabbing, and scarring occur due to cellular hypersensitivity to UV radiation. Precancerous lesions, actinic keratoses, and malignant skin tumors develop in childhood and adolescences.

About 12–50% of patients with xeroderma pigmentosum have visual impairment due to ocular changes. Ocular tissues with direct light exposure including the eyelids, conjunctiva, and cornea are most affected. More than 80% of patients will have benign and/or malignant lesions on the eyelids including hyperpigmented lesions, basal cell carcinomas, or squamous cell carcinomas. Other ocular findings include keratitis, band keratopathy, pterygium, and corneal scarring, ulceration, neovascularization, and perforation. Malignant neoplasms of the ocular surface can also occur, including squamous cell carcinoma, basal cell carcinoma, and melanomas. Patients usually have extreme photophobia.

Diagnosis

Diagnosis can be confirmed by molecular analysis by performing DNA-repair tests after UV exposure on a skin biopsy. DNA sequencing can also be done to determine specific mutations in the DNA-repair genes.

Differential Diagnosis

Xeroderma pigmentosum must be distinguished from other DNA-repair deficiency syndromes such as Cockayne syndrome and trichothiodystrophy that also present with extreme light sensitivity and autosomal recessive inheritance. Cockayne syndrome has characteristic neurological symptoms with distinct facies and weight loss. Trichothiodystrophy is characterized by dwarfism, brittle short hair, and ichthyoses.

Prophylaxis

Prenatal diagnosis by analyzing amniotic cells is possible.

Therapy

The main therapy for xeroderma pigmentosum is prevention by absolute avoidance of sunlight and other UV light exposure. Use of sun block and UV-blocking clothing, hats, and eyewear is recommended. Patients may benefit from switching day-night cycles. Close monitoring by dermatologist, ophthalmologists, and dentists for early identification and removal of neoplasms is necessary.

Prognosis

Prognosis is poor. Patients with xeroderma pigmentosum have a 1,000 times higher risk of tumor incidence. About two-thirds of patients die before reaching adulthood due to metastatic disease.

Epidemiology

Xeroderma pigmentosum is a rare autosomal recessive disorder that occurs equally in males and females. Prevalence is higher with consanguinity. Incidence is estimated at 1:250,000 live births in Europe and North America and 1:40,000 live births in Japan.

Cross-References

- ▶ Basal Cell Carcinoma of Eyelid
- ▶ Squamous Cell Carcinoma of Eyelid
- ▶ Squamous Cell Carcinoma, of the Conjunctiva

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Xerophthalmia

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Synonyms

Vitamin A deficiency

Definition

Xerophthalmia refers to the spectrum of ocular disease caused by vitamin A deficiency, and it is a late manifestation of severe deficiency of this nutrient.

Etiology

Vitamin A is a fat-soluble vitamin that is involved in corneal metabolism. Additionally, specific retinol-binding proteins are present in the epithelium, keratocytes, and endothelium of the cornea. The mechanism by which xerophthalmia develops is unclear, but the role of vitamin A deficiency in xerophthalmia is clear. The liver is able to store a 1–2-year supply of vitamin A under normal conditions. When vitamin A intake exceeds 300–1200 mg/day of retinol or an equivalent, the liver lays down stores of the vitamin. However, when intake falls before this level, the stores are depleted in order to maintain serum retinol levels above 0.7 mmol/L (Paranjpe et al. 2011). Vitamin A can be found in animal and dairy products, usually in the form of retinyl palmitate. Carotene is a naturally occurring precursor to vitamin A, which is produced by plants. The most important of the carotenoids is beta-carotene, which is found is dark-green leafy vegetables and some colored fruits (Kent and Jakobiec 2008).

Lack of vitamin A may be secondary to malnutrition, malabsorption, and chronic alcoholism. Infants are at increased risk for xerophthalmia if

their mothers are malnourished and by coexisting diarrhea or measles (Kanski and Bowling 2011). Systemic diseases associated with vitamin A deficiency affect its absorption or metabolism, including sprue, Crohn's disease, cystic fibrosis, abetalipoproteinemia, and pancreatic insufficiency. Surgical procedures, such as jejunoileal bypass, can be causes of vitamin A deficiency and eventual xerophthalmia (Kent and Jakobiec 2008). Measles (rubeola virus) is closely associated with vitamin A deficiency. Xerophthalmia secondary to measles keratoconjunctivitis was a significant issue until the mid-twentieth century in Europe and continues to be a devastating disease in developing countries (Paranjpe et al. 2011).

Deficiencies of fats or proteins involved in the metabolism of carotene and vitamin A can lead to xerophthalmia as well, but they tend to play a minor role. Vitamin A deficiency usually occurs in conjunction with generalized protein-energy malnutrition (PEM), which has raised uncertainty as to which factor is more significant in corneal disease. The malabsorption seen in PEM may cause reduced retinol levels directly and by impairment in beta-carotene conversion. Reduced protein synthesis prevents vitamin A release from the liver. Therapy with high doses of vitamin A has been shown to stimulate healing in cases of xerophthalmia despite the presence of severe PEM, which would support the significance for vitamin A as a factor in corneal disease (Paranjpe et al. 2011).

Clinical Presentation

Xerophthalmia causes changes in mucosal surfaces throughout the body, including the eye. Other organ systems affected include the epithelium of the lungs and the intestine, which undergo keratinizing metaplasia (Paranjpe et al. 2011). Xerophthalmia may present with night blindness (nyctalopia), ocular discomfort, and vision loss. Children with vitamin A deficiency are likely suffering from systemic illnesses, including diarrhea, respiratory illness, and measles (Vaddavalli et al. 2011). A grading scheme has been devised to classify different stages of the disease. The WHO grading scheme remains the standard for assessment for xerophthalmia (Kanski and Bowling 2011).

XN: night blindness
X1A: conjunctival xerosis
X1B: Bitot's spots
*X*2: corneal xerosis
X3A: corneal ulceration, less than one-third
X3B: corneal ulceration, more than one-third
XS: corneal scar
XF: xerophthalmic fundus

Night Blindness (XN)

Night blindness is one of the earliest symptoms of xerophthalmia. Mild cases of nyctalopia or night blindness may only be apparent after photic stress. Histologically, photoreceptor degeneration may be observed in the outer segment (Kent and Jakobiec 2008). Retinol is essential for the production of rhodopsin, a visual pigment produced by the rod photoreceptors. All patients respond rapidly to therapy with vitamin A, typically within 48 h (Paranjpe et al. 2011).

Conjunctival Xerosis (X1A) and Bitot's Spots (X1B)

Xerosis is characterized by dryness of the conjunctiva, particularly of the interpalpebral zone. Histologically, xerosis results in loss of goblet cells, squamous metaplasia, and keratinization (Kanski and Bowling 2011). Though histologic evidence of xerosis is present throughout the conjunctiva in the early stages of the disease, it is typically only clinically apparent in the temporal conjunctiva. The nasal and inferior conjunctivas are next to show clinical evidence. The superior conjunctiva shows clinical evidence in the later stages of the disease (Paranjpe et al. 2011). Conjunctival xerosis signifies mild disease, but corneal xerosis implies more severe deficiency (Vaddavalli et al. 2011). Once excised, if an adequate diet is maintained, the lesions do not recur (Paranjpe et al. 2011).

Bitot's spots appear as triangular patches of foamy keratinized epithelium in the interpalpebral zone (Kanski and Bowling 2011). Histologically, they are seen as tangles of keratin with saprophytic bacteria and occasionally fungi. The

material can easily be scraped off, but the base remains xerotic and the spot tends to recur within a few days. It may involve the cornea and the conjunctiva and can be quite extensive. Bitot's spots were first observed as dry scaly patches on the bulb of the eye. They were seen in association with nyctalopia and lackluster corneas. However, Bitot's spots have been observed in isolation and been nonresponsive to vitamin A therapy, suggesting that they may not be associated with vitamin A deficiency. *Corynebacterium xerosis* has been identified in Bitot's spots, and it has been suggested that it may be responsible for their typical foamy appearance (Paranjpe et al. 2011).

Nasally situated spots have been identified as more reliable indicators of active vitamin A deficiency, and they are always less prominent than temporal spots. Additionally, age is a more significant indicator of deficiency. In children under the age of 6 years, 97% of the lesions resolve rapidly. However, individuals over the age of 10 years are unresponsive in 60% of cases. Dryness of the conjunctiva should always be considered significant in children (Paranjpe et al. 2011).

Corneal Xerosis (X2)

The cornea may exhibit a lusterless appearance due to secondary xerosis. Vitamin A deficiency has been found to reduce aqueous tear production, and the loss of goblet cells leads to localized drying of the epithelium. Superficial punctate epithelial erosions may develop in xerophthalmia, initially seen inferonasally and later spreading to affect the entire corneal epithelium (Paranjpe et al. 2011). Bilateral punctate corneal epithelial erosions in the interpalpebral zone may progress to larger epithelial defects (Kanski and Bowling 2011). Occasionally, water-repellant microcysts that do not stain with fluorescein are observed. However, these changes are reversible with vitamin A therapy. Keratinization of the corneal epithelium may occur, causing the epithelium to take on a peau d'orange appearance. Pooling of fluorescein dye between keratinized epithelial plaques may give the epithelium a tree bark appearance (Paranjpe et al. 2011).

Corneal Ulceration and Keratomalacia (X3A/X3B)

Uncomplicated ulcers may develop in xerophthalmia, which typically have sharp margins. Rupture of subepithelial bullae may cause superficial ulcers of varying depths, which tend to form in the lower half of the cornea. Superficial ulcers tend to heal with minimal scarring (Paranjpe et al. 2011). Severe lesions may develop sterile corneal melting by liquefactive necrosis known as keratomalacia, which can lead to perforation of the cornea (Kanski and Bowling 2011). Secondary infection may develop and often leads to permanent blindness (Vaddavalli et al. 2011). The ulcers are typically gray or yellow in color and vary in size from 2 mm to involvement of the entire cornea. They may appear elevated, but collapse to reveal stromal loss with sharp boundaries following treatment. Deep stromal loss produces descemetoceles, which rupture easily under pressure. Rupture frequently results in scarring and formation of anterior staphylomata (Paranjpe et al. 2011).

Retinopathy

Xerophthalmia may also cause retinopathy characterized by yellowish peripheral dots with irregular borders. Retinopathy typically occurs in advanced cases, and it is associated with decreased electroretinogram amplitude (Kanski and Bowling 2011).

Diagnosis

The diagnosis of xerophthalmia is clinical and does not require any additional workup. When the diagnosis is in doubt, cytology of the superficial layers of the conjunctival epithelium may reveal loss of goblet cells and keratinization of epithelial cells (Prajna and Rajamani 2013). Dark adaptation, electroretinographic findings, and visual fields are all abnormal in early cases manifesting as night blindness (Vaddavalli et al. 2011).

Differential Diagnosis

The differential diagnosis for xerophthalmia includes Sjögren's syndrome, age-related

hyposecretion, lacrimal tissue destruction or obstruction, chemical ocular trauma, neurologic lesions with sensory or motor reflex loss, meibomian gland dysfunction, lagophthalmos, contact lens wear, and environmental conditions leading to dry eye (Kanski and Bowling 2011).

Prophylaxis

Improving vitamin A status of all deficient individuals, particularly children, could prevent one to three million deaths annually. The cost of vitamin A supplementation for 2 days costs approximately 10 cents per child. Measles immunization can prevent infection, which is a known risk factor for vitamin A deficiency (Paranjpe et al. 2011).

Therapy

The diagnosis of xerophthalmia should be treated promptly with massive supplementation of vitamin A. The development of keratomalacia indicates very severe vitamin A deficiency, and it should be treated as a medical emergency due to the associated risk of death, particularly in infants. Systemic treatment involves oral (oil-based 200,000 IU) or intramuscular (aqueous-based 100,000 IU) supplementation of vitamin A -(Kanski and Bowling 2011). Standard dosing by the World Health Organization varies with age. In children over 12 months of age and all women of childbearing age, oral therapy is preferred, which can be administered as 110 mg retinol palmitate or 66 mg retinol acetate (200,000 IU) given immediately and again the following day. Another dose should be given 2 weeks later to boost liver reserves of the vitamin (Paranjpe et al. 2011).

If parenteral replacement is indicated, such as in cases of severe anorexia, edematous malnutrition, septic shock, or inability to take oral supplementation, 55 mg of water-miscible retinol palmitate can replace the first dose. One-half the dosage is indicated in children aged 6–12 months. In children younger than 6 months, one-quarter of the dosage is appropriate. Multivitamin supplements and dietary sources of vitamin A should also be administered. Protein-deficient individuals should receive adequate treatment for PEM, and vitamin A supplementation should continue every 1–2 weeks until PEM correction is achieved (Paranjpe et al. 2011).

Women of reproductive age with night blindness or Bitot's spots should be treated with 5,000–10,000 IU daily for 4 weeks. Alternatively, a weekly dose of 25,000 IU may be administered. However, supplementation should be avoided in pregnancy to prevent teratogenesis. Instead, the mother should be given 400,000 IU at childbirth to increase the level of vitamin A provided to her infant via breast milk. Children at high risk should receive repeat dosing every 4–6 months. A priming dose given 1 week before the full dose can extend the protection provided (Paranjpe et al. 2011).

Local treatment involves aggressive lubrication. Topical retinoic acid may be used to promote healing, but it does not provide adequate treatment without systemic supplements. Corneal perforations should be addressed surgically with primary corneal grafting or amniotic membrane transplantation (Kanski and Bowling 2011).

Prognosis

Night blindness typically responds well to treatment with vitamin A supplementation (Kent and Jakobiec 2008). Prompt treatment of a corneal ulcer or keratomalacia involving less than one-third of the corneal surface often restores vision given the visual axis is usually unaffected. Treatment in cases of more extensive corneal involvement may prevent globe rupture and preserve useful vision in the contralateral eye (Paranjpe et al. 2011). However, the presence of keratomalacia indicates severe deficiency and a poor prognosis. More than 50% of children with xerophthalmia die due to poor nutritional status and susceptibility to disease (Vaddavalli et al. 2011).

Epidemiology

An estimated 140 million children worldwide are vitamin A deficient, second only to protein-calorie

malnutrition in prevalence. Of these children, 4.4 million are xerophthalmic. Approximately 250,000–500,000 xerophthalmic children become blind each year, and up to half of them will die within a year of losing their vision. Young infants depend upon the vitamin A supplied by their mother's milk, which decreases over time. Thus, children between 6 months and 3 years of age are most at risk of blinding corneal disease (X2, X3). It is estimated that 7.2 million pregnant women is vitamin A deficient and 13.5 million have reduced vitamin A levels. Over 6 million pregnant women develop night blindness, particularly during their third trimester when maternal and fetal demands are greatest. Older children, between 3 and 6 years of age, are more at risk of conjunctival disease, due to nutritional deficiencies. Xerophthalmia is particularly prevalent in Southeast Asia where rice is a staple food. Areas of endemic xerophthalmia have a diet deficient in preformed vitamin sources, such as milk, eggs, and meats, and provitamin sources are relied on more heavily (Paranjpe et al. 2011). Malnourished children with low vitamin A levels often become xerophthalmic after contracting measles (Vaddavalli et al. 2011). Though xerophthalmia largely affects impoverished individuals in developing countries, it can occur occasionally in developed nations as well. It has been observed in food faddists, psychiatric patients, and chronic alcoholics (Paranjpe et al. 2011).

Cross-References

- ▶ Beta Carotene, Use and Dosage of
- ▶ Nyctalopia: Night Blindness

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Xerosis

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Synonyms

Conjunctival xerosis

Definition

Xerosis refers to the extreme ocular dryness and keratinization that occurs in eyes with severe conjunctival cicatrization (Kanski and Bowling 2011).

Etiology

Xerosis may occur secondary to keratoconjunctivitis sicca, ocular pemphigoid, trachoma, measles, vitamin A deficiency, exposure proptosis, chemical burns, and Stevens-Johnson syndrome (Yanoff and Sassani 2015).

Clinical Presentation

Patients may present asymptomatic with xerosis or with symptoms such as redness, dryness, itching, foreign body sensation, and pain (Khurana 2008). Severe damage may result in ulceration.

Diagnosis

The diagnosis of dry eye and xerosis is made primarily by patient history and physical exam.

Excessive reflex tearing and sensation of itching, burning, redness, and irritation are helpful in determining if a patient has experienced dry eye (Gupta et al. 2006). Ocular staining with agents such as lissamine green may be used to determine extent of dryness and possible corneal damage. Further, testing can include a Schirmer's tear test and tear film break-up time.

Patients with vitamin A deficiency may present with Bitot's spots, which are superficial keratin accumulations on the conjunctiva (Shukla and Behari 1979).

Histologically, the epithelium undergoes epidermidalization with keratin formation, and the underlying subepithelial tissue frequently shows cicatrization (Yanoff and Sassani 2015).

Differential Diagnosis

Deficient lid closure, vitamin A deficiency, congenital tear reduction, Sjogren syndrome, medication side effect.

Prophylaxis

If nutrient related, vitamin A supplementation may benefit patients (Kiegman et al. 2011). Avoiding triggers (medications) as well aids in preventing xerosis. Tear preparations may help patients as well as prevent xerosis.

Therapy

Treatment of xerosis involves treating the initial cause of the dry eyes. Symptomatic treatment may involve artificial tear preparations (0.7% methyl cellulose or 0.3% hyperomellose or polyvinyl alcohol) (Khurana, 2008).

Prognosis

Prognosis is positive for patients who continue with medical management and follow-up to limit progression of corneal and conjunctival disease secondary to dry eye and xerosis (Khurana 2008). Lack of care from dry eye may result in ulceration and ocular damage.

Epidemiology

Xerosis may affect patients of all ages and genders. It has been found to be associated with patients with vitamin A deficiency (Kiegman et al. 2011).

Cross-References

► Dry Eye Syndrome

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X-Linked Incomplete Achromatopsia

► Blue Cone Monochromatism

X-Linked Megalocornea

► Anterior Megalophtalmos

Y

Y-V Medial Canthoplasty

► Y-V-Plasty for Blepharophimosis Syndrome

Y-V-Plasty for Blepharophimosis Syndrome

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Synonyms

Medial canthoplasty; Medial epicanthoplasty; Y-V medial canthoplasty

Definition

Generally speaking, Y-V-plasty is a reconstructive surgical technique which can be utilized for the modification of contracted scars. In the realm of ophthalmic plastic surgery, it can be used more specifically for the repair of telecanthus and epicanthus associated with the blepharophimosis syndrome.

Indication

Y-V plasty is indicated in the surgical correction of mild/moderate telecanthus and epicanthus in blepharophimosis syndrome. The technique may be combined with other techniques such as local transposition flaps (as in the Mustarde modification) and transnasal wiring if more severe telecanthus and epicanthus exist.

Contraindications

An alternative or combined approach may be required in addition to Y-V-plasty if there is a significant degree of epicanthus and/or telecanthus.

Techniques and Principles

A horizontally oriented Y shaped incision is made at the medial canthus, with the base of the Y positioned at the desired new position of the medial canthus. The skin flaps are elevated to allow mobilization. Subcutaneous tissue is often

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thickened and can be conservatively thinned to create the appearance of the medial canthal depression. Depending on the severity of the telecanthus, the surgeon can access and tighten the anterior limb of the medial canthal tendon during surgery. If desired, the anterior limb of the medial canthal tendon is disinserted from the periosteum, advanced medially, and reattached to more medially positioned periosteum. This results in medialization of the medial canthus and reduction of telecanthus. The skin is closed with suture of the surgeon's choice. The technique may be combined with other techniques such as local transposition flaps (as in the Mustarde modification) and transnasal wiring if more severe telecanthus and epicanthus exist.

Outcome

The net effect of the Y-V-plasty in the medial canthus is recruitment of tissue in the vertical plane perpendicular to the medial canthal tendon and shortening of tissue in the horizontal plane parallel to the medial canthal tendon. This results in improvement of telecanthus and epicanthus with V-shaped surgical scar at the medial canthus.

Complications

Flap necrosis and poor wound healing may result, particularly if excess tension on the wound exists. Use of the Y-V-plasty technique alone in severe telecanthus may result in recurrent telecanthus and phimosis of the medial canthus if significant postoperative tension is present.

Cross-References

- ▶ Bridge Flap Technique
- ▶ Telecanthus
- ▶ Z Plasty

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Z

Z Plasty

► Transposition Flaps, for Lateral Canthal Defects

Zeis Gland Cyst

► Chalazion

Zellweger Syndrome

► Cerebrohepatorenal (Zellweger) Syndrome

Zernike Coefficients

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Synonyms

Wavefront aberration coefficients

Definition

A Zernike coefficient is the coefficient that represents each Zernike polynomial in the wavefront function (Zernike reconstruction).

Basic Characteristics

The reconstruction of the human eye's wavefront with Zernike polynomials is widely accepted both in physiological optics and clinical practice (Thibos et al. 2002). Zernike polynomials are a set of orthogonal functions over the unit circle, each polynomial describing a certain surface shape. Irregular surface shapes such as the ocular wavefront or the corneal surface can be reconstructed efficiently by creating a summary function of Zernike polynomials. The addition of a set of polynomials creates a new surface. The dominance of each polynomial in the summary function is indicated by a coefficient – the Zernike coefficient – that weights the polynomial within the function. The more the coefficient is different from Zero, the more the shape of the wavefront is dominated by the certain polynomial. The full set of Zernike coefficients equals a numerical representation of the reconstructed wavefront, comparable to the CMYK or RGB representation of a color. Zernike coefficients are only valid over a given pupil diameter (PD). For other PDs than the given, the coefficients need to be recalculated. While down-scaling to a smaller PD can be achieved mathematically, an up-scaling to a larger PD involves extrapolation and leads to probably invalid results.

Zernike coefficients are numerical values, typically with the unit micrometers [μm]. The sign can be positive or negative. Change of sign of rotationally symmetric polynomials results in a

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flip along the frontal plane, change of sign of cosine phase polynomials results in a flip along the horizontal plane, and change of sign of sine phase polynomials results in a flip along the vertical plane. The nomenclature for Zernike coefficients equals the nomenclature for Zernike polynomials with the letter C instead of Z. In clinical practice, C and Z are often used synonymously. Also for Zernike coefficients, a double (C_n^m) or single index scheme can be used (C_n). Coefficients of the same order or homologous coefficients can be condensed to root mean square (RMS) values that quantitatively describe the wavefront aberration. RMS values cannot be negative.

The contribution of each Zernike mode to visual function remains to be determined. Each mode tends to interact with the other modes in the wavefront function; therefore it is difficult to define critical values for each coefficient (Applegate et al. 2002). From Zernike coefficients, the point spread function (PSF) and modulation transfer function (MTF) and corresponding image quality metrics can be computed using Fourier transformation.

Zernike coefficients represent the basis data generated by wavefront sensors. They can be used for further computations such as wavefront maps, RMS values, image quality metrics, and construction of wavefront-guided ablation profiles.

Cross-References

- ▶ Optical Aberrations
- ▶ Wavefront Measurement

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Zoster

▶ Herpes Zoster

Z-Plasties

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Synonyms

Rotational advancement flap; Transposition flap

Definition

Z-plasty is a reconstructive surgical technique utilizing transposition flaps to release tension and contracture of scars and to redirect scars into more favorable orientations.

Indication

Z-plasty has extensive applications in plastic and reconstructive surgery of the face and eyelids. Broadly speaking, however, it can be utilized to achieve several basic outcomes: release of and lengthening of a contracted scar, reorienting a scar to fall within relaxed skin tension lines, and dispersion of a scar. More specifically, the technique can be utilized for: revision of facial scars; surgical modification of eyelid scars, for example, scars resulting in cicatricial ectropion; management of epicanthal folds and telecanthus, for example, in blepharophimosis syndrome; and correction of symblepharon.

Contraindications

Large scars may limit the ability to achieve tension-free closure which can result in flap necrosis and contraction.

Techniques and Principles

The classic z-plasty technique is comprised of three incisions of equal length. The central incision lies in the long axis of the scar parallel to the plane of tension. This incision becomes the central arm of the Z. The second and third incisions are made at opposite ends of the central incision and at an angle of 60° to the central incision and become the arms of the Z. Modifications exist where the angles utilized are more or less than 60°; however, the classic Z-plasty utilizes 60° angles as described. The three incisions are of equal length and the result is two equilateral triangle shaped flaps that are mirror images. Undermining of the flaps with scissors is performed until the scar contracture bands are lysed and the flaps are able to be transposed without tension. The tips of the flaps are then transposed. Multiple deep-buried absorbing sutures are placed to reduce tension and the skin is then closed.

Outcome

Z-plasty results in reorientation, lengthening, and dispersion of a scar; reduction in scar contracture and tension; and a z-shaped surgical scar as a final result.

Complications

Flap necrosis and poor wound healing may result, particularly if excess tension on the flaps exists.

Cross-References

- ▶ Eyelid Reconstruction
- ▶ Symblepharon
- ▶ Tarsal Fracture Operation, for Cicatricial Entropion
- ▶ Y-V-Plasty for Blepharophimosis Syndrome
- ▶ Z Plasty

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Zygomatic Bone

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Synonyms

Cheekbone; Malar bone

Definition

The zygomatic bone articulates with the sphenoid bone, maxilla, frontal bone, and temporal bone to form the lateral wall of the floor of the orbit, part of the temporal and infratemporal fossa, and the prominence of the cheek.

Structure

The anatomy of the zygomatic bone is composed of two surfaces, four processes, and four borders.

The malar surface of the zygomatic bone is perforated near its center, which gives rise to the zygomaticofacial foramen. Slightly below this foramen is an elevation, which serves as the origin to the zygomaticus. At the center of the temporal surface of the zygomatic bone is the zygomaticotemporal foramen. The medial part of the temporal surface articulates with the maxilla, while the lateral upper part forms the anterior boundary of the temporal fossa and the lateral lower part forms the boundary of the infratemporal fossa.

The frontosphenoidal process of the zygomatic bone articulates with the zygomatic process of the frontal bone. Approximately 11 mm below the zygomaticofrontal suture and 2 mm behind the lateral orbital rim is the Whitnall's tubercle, which is the site of attachment for the lateral canthal tendon that provides the eyelid contour. The orbital process forms part of the floor of the lateral wall of the orbit by articulating with the orbital surface of the maxilla and the greater wing of the sphenoid. On the floor of the lateral wall of the orbit is the zygomatico-orbital foramen, which is a set of two canals. One of these canals opens on the temporal surface, making up the zygomaticotemporal foramen, and the second of these canals opens on the malar surface, making up the zygomaticofacial foramen. The maxillary process articulates with the maxilla, the temporal process with the zygomatic process of the temporal bone.

The orbital border forms part of the orbital circumference. The maxillary border articulates with the maxilla, and near the orbital margin, it gives rise to the quadratus labii superioris. The temporal border is continuous with the temporal bone and the zygomatic arch. The zygomatic border is attached to the masseter.

Function

The zygomatic bone functions as an integral part that makes up several other important structures, including the zygomatico-orbital, zygomaticotemporal, and zygomaticofacial foramen which transmit respective branches of the maxillary nerve (V2) and vasculature. The zygomatic bone also forms the lateral wall of the floor of the orbit, part of the temporal and infratemporal fossa, and the prominence of the cheek.

Clinical Relevance

Zygomatic fractures are the second most common fractures of the facial bones, and as much as 5% of patients with zygomatic fractures have associated ophthalmic injury (Covington et al. 1994). Due to its prominence, the zygomatic bone is prone to fractures from direct trauma to the side of the face. Zygomatic fractures can involve the zygomaticofrontal, zygomaticomaxillary, and zygomatic arch, with fractures involving all three regions being the most common (Hwang and Kim 2011). Since the zygomatic bone contains both the zygomaticotemporal and zygomaticofacial foramen with their respective nerves, zygomatic fractures commonly lead to anesthesia of the cheek and side of forehead. The zygomatic bone also serves as the insertion for the masseter, and zygomatic fractures can therefore lead to difficulty with mastication. Zygomatic fractures can lead to binocular diplopia due to muscle entrapment in the orbital cavity or neuromuscular injury.

The zygomatic bone also serves as an important landmark for several surgeries, including maxillofacial and orbital procedures, which involve osteotomies across the zygomatic bone (Loukas et al. 2008). Vascular and neoplastic lesions at the skull base can be exposed through an orbitozygomatic osteotomy approach, which involves five cuts to free the orbitozygomatic bone in one piece above the zygomaticofacial foramen. Excision of infraorbital tumors as well as orbital decompression can also be achieved through transmaxillary surgical approaches to the orbit.

Cross-References

▶ Zygomaticofacial Canal
▶ Zygomaticotemporal Canal

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Zygomatic Complex Fracture

► Zygomatic-Maxillary Complex Fractures

Zygomatic-Maxillary Complex Fractures

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Synonyms

Malar complex fracture; Maxillary complex fracture; Orbito-zygomatico-maxillary fracture; Tetrapod fracture; Trimalar fracture; Tripod fracture; Zygomatic complex fracture

Definition

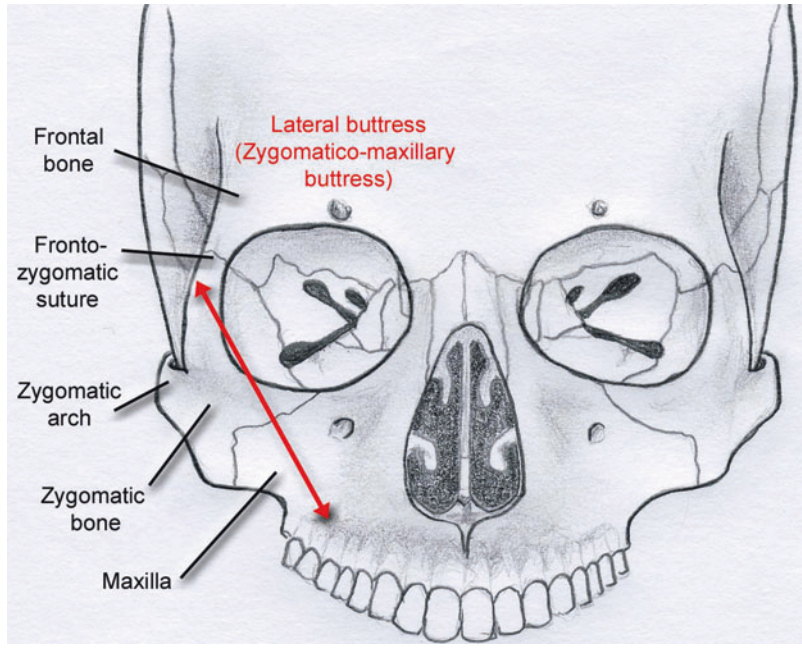
The most common zygomatico-maxillary complex (ZMC) fracture pattern involves fracture of the frontozygomatic suture (lateral orbital rim), the zygomatic arch, the lateral buttress (zygomatico-maxillary buttress), and the inferior orbital rim (Cummings 2005). The fractures through the lateral buttress and the inferior orbital rim are commonly connected by an anterior maxillary wall fracture. Although this represents the most common fracture pattern, significant variation exists. For example, the zygoma itself may be fractured into pieces and partial ZMC fractures, involving some, but not all of the fractures listed above, may occur (Figs. 1 and 2).

Etiology

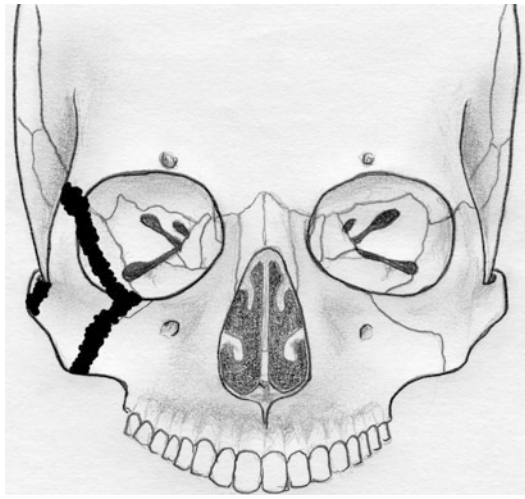
Motor vehicle accidents, interpersonal altercations, assaults, falls, and sports-related injuries.

Clinical Presentation

The zygomatic complex plays a key role in midfacial contour and protection of orbital contents and has many important relationships to surrounding soft tissue structures that influence the clinical signs of a ZMC fracture (Della Rocca et al. 2002). The masseter muscle attaches to the zygoma, and its unopposed force on the mobile bone fragment after ZMC fracture is responsible for the inferior displacement and medial rotation of the malar process. This displacement is appreciated clinically as flattening of the malar eminence. The temporalis muscle inserts on the coronoid process of the mandible and travels beneath the zygomatic arch to its attachment on the temporal bone superiorly. Depressed ZMC fractures can exert pressure on the temporalis muscle, causing trismus and severe pain with mastication. The lateral canthal tendon attaches to the inner aspect of the lateral orbital rim at Whitnall's tubercle. Inferior displacement of the zygoma after a fracture may result in displacement of the lateral canthus. Step-offs on the lateral or inferior orbital rims may often be palpated. Fractures may pass through, or close to, the infraorbital foramen, resulting in anesthesia of the infraorbital nerve distribution.



Zygomatic-Maxillary Complex Fractures, Fig. 1 Important anatomic correlates in ZMC fractures.



Zygomatic-Maxillary Complex Fractures, Fig. 2 Typical location of a ZMC fracture.

Significant facial edema is common, and it is important to investigate for additional maxillofacial injuries. The presence of diplopia or difficulty with eye movements may indicate extraocular muscle pathology (e.g., entrapment). Change in globe positioning, often in the form of enophthalmos, may occur.

Diagnostics

Facial fractures often occur as the result of significant trauma and evaluation should begin with airway control and homodynamic stabilization. Spinal cord injury should be ruled out. A thorough history and physical, including a complete head and neck, exam may then be performed. With any midfacial fracture, suspicion for CSF rhinorrhea and/or otorrhea should be high. ZMC fractures involve orbital wall fractures, and the eye must be completely evaluated (Holck and Ng 2006). Examination of dental occlusion is also important, as fractures can extend through the maxillary alveolus, resulting in malocclusion. Facial radiographs, particularly the submental vertex view, may suggest the diagnosis, but maxillofacial CT scan is considered the modality of choice for diagnosis of ZMC fractures.

Differential Diagnosis

Orbital floor (blowout) fracture, nasal bone fracture, naso-orbital-ethmoid fracture, LeFort fracture, and maxillary (Guerin) fracture.

Prophylaxis

The use of restraints, seat belts, and protective headgear can help prevent ZMC fractures.

Therapy

ZMC fractures in which the zygoma is nondisplaced and ophthalmologic examination is normal can be treated conservatively with analgesia, soft diet, and close follow-up. Indications for surgical reduction and fixation of a ZMC fracture are cosmetic deformity resulting from inferior and medial displacement of the zygoma, trismus, pain with chewing, enophthalmos, diplopia, or gaze restriction (Kelly et al. 2007). Stable surgical repair often requires fixation of at least two fracture sites, most commonly the frontozygomatic suture line and the zygomatico-maxillary buttress (Stewart 2005). Care must be taken to avoid postoperative enophthalmos, as reduction of the zygomatic fracture may accentuate an already-present orbital floor fracture, requiring orbital floor plating. Perioperative antibiotics should be considered in patients with facial fractures. Patients with ZMC fractures that are not displaced on initial presentation should be followed closely to assure that the fracture does not become displaced with time.

Prognosis

Long-term prognosis after repair of ZMC fracture is excellent. Postoperative infection rates are low and generally resolve with oral antibiotics. Facial asymmetry necessitating revision surgery after initial repair occurs in 3–4% of patients.

Epidemiology

ZMC fractures are the second most common midface fracture, after nasal fractures. Eighty percent of ZMC fractures occur in males and 80% of ZMC fractures occur between the ages of 18–45, with peak incidence between 20 and 30 years of age. Assault is responsible for the majority of ZMC fractures (40%), followed by sports injuries, MVA, and falls.

Cross-References

- ▶ Blowout Fractures
- ▶ Guerin (Maxillary) Fracture
- ▶ Le Fort Fractures
- ▶ Maxillary Fractures
- ▶ Naso-Orbital-Ethmoid Fractures
- ▶ Orbital Floor Fracture
- ▶ Spiral Computed Tomography, in Orbital Evaluation
- ▶ Three-Dimensional Computed Tomography, in Orbital Evaluation
- ▶ Zygomatic Bone

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Zygomaticofacial Canal

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Definition

The zygomaticofacial canal arises from the zygomatico-orbital foramen and transmits the

zygomaticofacial nerve, which supplies the malar surface.

Structure

The zygomaticofacial canal arises from the zygomatico-orbital foramen and plays a vital role in transmitting the zygomaticofacial nerve. The zygomatic nerve enters the orbit through the inferior orbital fissure and divides in the back of the orbital cavity into the zygomaticofacial and zygomaticotemporal nerves. The zygomaticofacial nerve courses, along the infero-lateral angle of the orbit, enter the zygomatico-orbital foramen and into the zygomaticofacial canal, which transmits the nerve through the zygomaticofacial foramen on the zygomatic bone. The zygomaticofacial nerve then perforates the orbicularis oculi and joins with the zygomatic branches of the facial nerve and with the inferior palpebral branches of the maxillary nerve to supply the malar surface, i.e., the skin on the prominence of the cheek.

Function

The zygomaticofacial canal functions as an intermediary between the zygomatico-orbital foramen and the zygomaticofacial foramen to transmit the zygomaticofacial nerve, which supplies the prominence of the cheek.

Clinical Relevance

The zygomaticofacial canal and foramen can be disrupted during zygomatic fractures, which are the second most common fractures of the facial bones (Covington et al. 1994). Due to its prominence, the zygomatic bone is prone to fractures from direct trauma to the side of the face. Zygomatic fractures can involve the zygomaticofrontal, zygomaticomaxillary, and zygomatic arch, with fractures involving all three regions being the most common (Hwang and Kim 2011). Since the zygomatic bone contains both the zygomaticotemporal and zygomaticofacial canals and foramen with their respective nerves, zygomatic fractures commonly lead to anesthesia of the cheek and side of forehead.

Surgeons operating in the maxillofacial and orbital regions should take great care not to injure the zygomaticofacial canal and foramen. External pin fixation is a commonly used technique for rigid fixation of bony fragments of zygomatic fractures. However, this procedure may cause midface paresthesia due to difficulty in identifying the zygomaticofacial canal and foramen, and inadvertent nerve damage. To avoid zygomaticofacial nerve damage, some surgeons have reported using open reduction and fixation with a miniplate, principally in the frontozygomatic suture (Kim et al. 2013).

Lastly, the zygomaticofacial canal and foramen also serve as important locations for local nerve blocks, which are important for operations in this region.

Cross-References

- ▶ Zygomatic Bone
- ▶ Zygomaticotemporal Canal

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Zygomaticotemporal Canal

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Definition

The zygomaticotemporal canal transmits the zygomaticotemporal nerve, which supplies the side of the forehead.

Structure

The zygomaticotemporal canal and foramen play a vital role in transmitting the zygomaticotemporal nerve. The zygomatic nerve enters the orbit through the inferior orbital fissure and divides in the back of the orbital cavity into the zygomaticofacial and zygomaticotemporal nerves. The zygomaticotemporal nerve courses, along the lateral wall of the orbit, receive a branch of communication from the lacrimal, and enter the zygomatico-orbital foramen and into the zygomaticofacial canal. While it was previously thought that the zygomatico-orbital foramen gave rise to both the zygomaticofacial and zygomaticotemporal canals, recent work has highlighted that the zygomaticotemporal canal arises from the zygomaticofacial canal (Kim et al. 2013). The zygomaticotemporal canal transmits the respective nerve to the temporal fossa through the zygomaticotemporal foramen. The zygomaticotemporal nerve ascends between the bone and temporalis muscle, perforates the temporal fascia approximately 2.5 cm above the zygomatic arch, and supplies the skin on the side of the forehead. As the zygomaticotemporal nerve pierces the temporal fascia, it gives off a branch that runs between the two layers of the fascia to the lateral angle of the orbit.

Function

The zygomaticotemporal canal functions as an intermediary between the zygomatico-orbital foramen and the zygomaticotemporal foramen to transmit the zygomaticotemporal nerve, which primarily supplies the side of the forehead.

Clinical Relevance

The zygomaticotemporal canal and foramen can be disrupted during zygomatic fractures, which are the second most common fractures of the facial bones. Due to its prominence, the zygomatic bone is prone to fractures from direct trauma to the side of the face. Zygomatic fractures can involve the zygomaticofrontal, zygomaticomaxillary, and zygomatic arch, with fractures involving all three regions being the most common. Since the zygomatic bone contains both the zygomaticotemporal and zygomaticofacial canals and foramen with their respective nerves, zygomatic fractures commonly lead to anesthesia of the cheek and side of the forehead.

Surgeons operating in the maxillofacial and orbital regions should take great care not to injure the zygomaticotemporal canal and foramen. For example, the zygomaticotemporal canal, foreman, and nerve may be injured during Gillies or Dingman reduction procedure for a zygomatic fracture, or during an endoscopic subperiosteal facelift (Hwang et al. 2004). The zygomaticotemporal nerve may also serve as a site of migraine genesis, and therefore surgical decompression of the temporalis muscle can aid in reducing migraines and their associated symptoms (Janis et al. 2010).

Cross-References

▶ Zygomatic Bone
▶ Zygomaticofacial Canal

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